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Title:
The cervix in pregnancy : an ultrasonographic investigation of the cervix and cervical change through pregnancy.

THE CERVIX IN PREGNANCY

An ultrasonographic investigation of the cervix and cervical change throughout pregnancy

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A dissertation submitted to the University of Bristol in accordance with the requirements of the degree of Doctor of Medicine in the Department of Obstetrics and Gynaecology within Faculty of Medicine

December 2000

Word Count: 25,233

Abstract

This study investigated the cervical appearance on transvaginal ultrasound throughout pregnancy. 275 women were scanned during pregnancy. Scans in the first trimester showed no difference in cervical appearance between those women with bleeding and those without, nor did the cervical length correlate with the gestation of delivery, but the numbers were too small to be conclusive.

In the second and third trimesters, two groups of women were investigated; those at high risk of a preterm delivery (n = 106) and those at low risk (n = 51). Measurements were taken of cervical length, width and opening of the internal os ("beaking"). Cervical width and beaking were of little value in predicting outcome. There was no difference in either groups in the cervical length in primiparous and multiparous women. A history of termination of pregnancy and a history of miscarriage were both associated with a short cervix in the high risk group. Multiple linear regression showed a past history of a preterm delivery, a short cervix and a shortening of the cervical length between 18 and 26 weeks were associated with an early delivery.

A small cohort (n = 11) within the high risk group had an open internal os at rest or after fundal pressure. Here cervical change was progressive over time, with a final cervical length under 10 mm, and the majority (78%) had amniotic membranes visible at the time of cervical cerclage. This appears to be the ultrasound picture of cervical incompetence.

Investigation of the cervix at and beyond term compared cervical length and Bishop score to the induction to delivery interval. In primiparous women only multiple linear regression showed cervical length to be an independent variable against the induction to delivery interval.

Acknowledgments

My thanks go to Mr Sanjay Vyas and Mr Phillip Smith for their support, advice and interest during my two years of research at Southmead Hospital. Also I am grateful for the support I received from the Antenatal and Early Pregnancy Clinic staff in hunting for patients and notes.

Finally, I must thank all the women who so readily took part in all the scanning, and also showed such an interest in the study. This MD is dedicated to them and their babies.

Author's Declaration

I delcare that the work in this dissertation was carried out in accordance with the Regulations of the Univiersity of Bristol. The work is original except where indicated by special reference in the test and no part of this dissertation has been submitted for any other degree.

Any views expressed in this dissertation are those of the author and in no way represent those of the University of Bristol.

The dissertation has not been presented to any other University for examination either in the United Kingdom or overseas.

Signed: Date:

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List of Abbreviations

ARM -	Artificial rupture of membranes
GAGs -	Glycosaminoglycans
ECMUS -	European Committee for Medical Ultrasound Safety
RCOG -	Royal College of Obstetricians and Gynaecologists
TVS -	Transvaginal scan
USS -	Ultrasound scan
WFUMB -	World Federation for Ultrasound in Medicine and Biology

Chapter 1

Introduction

This MD is the result of a 2 year research post at Southmead Hospital in Bristol. The research was started in December 1995 and continued until September 1997, during which time over 250 women were involved in investigation of the transvaginal appearance of the cervix throughout pregnancy. Approximately 1000 transvaginal scans were performed during this time. The original literature search covered the period up to the end of 1995, and this is what will be presented in the introduction to this thesis. At the end of each chapter covering differing aspects of the research, I will review the literature published subsequent to the completion of the thesis up until the end of 1999, and re-assess the work done during my research post in the light of the later published work.

"The cervix ... is perhaps best regarded as the frontier post between (the) two parts of the genital tract" (Calder and Greer 1992)

The division between the upper and lower genital tracts, the cervix has long been recognised as having a dual role, particularly in pregnancy; a barrier against the outside environment for the upper genital tract and its contents during pregnancy, whilst also acting as the passage for fetus and placenta, allowing delivery at the appropriate gestation but not before. Major changes occur in the cervix in pregnancy and labour in comparison to the non-pregnant state, and much has been determined regarding the histological and pharmacological changes (Calder and Greer 1992, Lopez Bernal et al 1994). However, investigation of the cervix in the clinical setting has been limited, and prediction of outcome using clinical measures such as the Bishop score (Bishop 1964) is poor. This study was designed to use transvaginal ultrasonography to observe and objectively monitor the cervix throughout pregnancy, with the aim of providing more detailed information about the pregnant cervix and the changes that occur both during normal and abnormal pregnancies.

Anatomy and Structure

The cervix uteri is the most caudal portion of the uterus, and in conjunction with the uterus develops embryologically from the two fused Mullerian ducts during the third month of development. In contrast to the uterine body, which is largely composed of smooth muscle fibres, the cervix has little muscle and is largely comprised of fibrous connective tissue. Collagen is the main component of the cervical connective tissue, with the majority (70%) being collagen type I and 30% type III (Danforth 1983). Other important contributors to cervical tissue are elastin and a ground substance largely comprised of glycosamnioglycans (GAGs); hydrophilic mucopolysaccharides such as dermatan sulphate, chondroitin sulphate and hyaluronic acid which are arranged with the collagen fibres and, depending on the particular GAG, alter the physical strength and rigidity of the cervix.

Cervical Changes in Pregnancy and Labour

This awareness of the cervical structure already gives some indication of the marked changes that occur in pregnancy and particularly in labour and delivery. A more than two-fold increase in the concentration of GAGs, and an increase in the proportion of hydrophilic GAGs in pregnancy leads to a softening of the cervix. Collagen concentrations reduce by up to 70% during pregnancy and particularly just prior to the onset of labour (Danforth 1974). Labour itself is associated with an increased activity of collagenase (produced by cervical fibroblasts) and elastase (produced by infiltrating neutrophils) and also a marked fall in the cervical GAG levels, which allows increased enzymatic activity on the collagen and also produces dissolution of the cervical connective tissue substance and reduced structural rigidity. The physiological processes which lead up to labour and delivery appear to progress over a period of four to five weeks prior to labour, with profound changes in cervical structure occurring during labour itself.

Endocrine changes play a significant part in cervical changes in pregnancy and labour. Progesterone has an inhibitory action on cervical ripening, probably through its anti-inflammatory properties by reducing the activity of neutrophils and by inhibiting the activity of the collagenase released. The importance of progesterone has been demonstrated with the effectiveness of the anti-progesterone Mifepristone (RU486) in promoting first and second trimester abortions by causing cervical ripening (WHO 1994). Oestrogen appears to have an opposite effect to progesterone, causing cervical ripening. Such an effect has been clearly demonstrated in sheep, with the rapid rise in oestrogen levels in sheep prior to labour. Although such a clear cut effect has not been demonstrated in humans, oestrogen is likely to be influential in cervical change during pregnancy and labour.

The final pathway for the alteration of the cervix through any mechanism appears to be via prostaglandins. The effectiveness of artificial cervical ripening and induction of labour using vaginal applications of prostaglandin E2 has been widely shown. Studies have shown the stimulation of prostaglandin production by oestrogen (Liggins et al 1977). The similarity between cervical change and an inflammatory process has been noted (Liggins 1981) and many known inflammatory mediators such as interleukin-1, interleukin-6 and tumour necrosis factor all appear in significant concentrations in the uterus and amniotic fluid at the onset of labour (Opsijln et al 1993).

In summary, significant changes in the cervical structure occur during pregnancy and particularly labour, producing the alterations seen as cervical effacement, softening and dilatation. The final mediator of cervical changes is prostaglandins, the production of which can be inhibited by progesterone and stimulated by oestrogen. However, numerous other inflammatory mediators are also present during normal labour at term.

Preterm Labour

Comparing preterm with term labour, the mechanisms of cervical change are similar, although the initiating factors may be different. Infection is thought to be a major contributor to pre-term labour, with abnormal vaginal colonisation being associated with pre-term delivery (Hay et al 1994a, Alger et al 1988). In those women with a threatened pre-term labour, a positive culture from an amniocentesis provides a strong indicator for failure of tocolysis and an early pre-term delivery (Romero et al 1993, Carroll et al 1995). Thus, there are similarities between the normal cervical changes seen in pregnancy and labour at term and the inflammatory response sometimes seen in preterm labour, hence it is not surprising that the physiological (and pathological) changes produced by an infection produce the same cervical changes as in labour at term; a marked rise in local prostaglandin production and release (Lopez Bernal et al 1989), a significant rise in the levels of inflammatory cytokines (Rath 1991, Romero et al 1993) producing cervical ripening and dilatation. On an experimental level, in threatened preterm labour, the presence of cytokines in amniotic fluid in large concentrations has been highly sensitive (81-100%) and specific (75-85%) in detecting the presence of an intrauterine infection, and in predicting a preterm delivery (Romero et al 1993, Greig et al 1993).

In summary, the final end point of labour preterm is the same as a normal labour at term, with prostaglandin production producing cervical change and uterine contractions, but the initiation can be via a different pathway; intrauterine infection producing a local release of inflammatory mediators and triggering the prostaglandin production. This does not explain all cases of preterm labour, but does provide an explanation of an alternative initiating sequence.

Clinical Investigation of the Cervix

In contrast with this extensive physiological information regarding cervical change in labour and the sensitivity of its prediction of labour and pre-term labour, clinical information about the state of the cervix and its accuracy of prediction of events outside labour itself is very limited. The most widely used assessment of the cervix, the Bishop score (Bishop 1964) employs the traditional examination of the cervix in terms of dilatation, effacement, cervical position and softness, and position of the fetal head. However, even when used as originally intended for cervical assessment prior to induction of labour, the Bishop score is not accurate in determining the ease of the induction. When applied, in conjunction with other parts of a clinical assessment, to threatened pre-term labour, cervical assessment is imprecise in diagnosing pre-term labour. An accuracy of between 30-80% has been suggested in making a correct diagnosis of pre-term labour when the clinician is presented with a woman in threatened pre-term labour (Kragt and Kierse 1990, O'Driscoll 1977, Turnbull 1989). At present clinical assessment of the cervix does not accurately predict the onset of labour.

Ultrasound in Obstetrics

The use of ultrasound in Obstetric practice started in the late 1950s and early 1960s, when Professor Donald in Glasgow used ultrasound to identify the intrauterine gestation sac and fetus (Donald 1961, Donald 1963). Since then ultrasound has been used very widely in Obstetrics; fetal viability and anomaly scanning, diagnosis of multiple pregnancy, monitoring of fetal growth, liquor volume measurements, placental siting, visualisation of intra-amniotic procedures such as amniocentesis, and in reproductive medicine, monitoring of ovulation induction treatment.

Originally, ultrasonography was performed transabdominally, providing excellent views of the fetus beyond 12 weeks gestation, but this was of limited use in visualising an early pregnancy, the non-pregnant uterus or the cervix. Development of the ultrasound probes over the past 10 years has produced probes small enough to be used rectally and vaginally, and transvaginal ultrasound has become an integral part of ultrasonography in early pregnancy, ovulation induction monitoring and gynaecology.

In the knowledge that clinical cervical assessment was insufficient to accurately predict pregnancy outcome several investigators have used ultrasound for observational studies of the cervix and cervical change during pregnancy and prior to labour, particularly with regard to pre-term labour and cervical incompetence (Table 1.1). Original research was performed using transabdominal ultrasound (Michaels et al 1986) but further studies showed transabdominal scanning, necessitating a full bladder to clearly visualise the bladder, produced artificially lengthened views of the cervix due to stretching around the distended bladder (Anderson et al 1990, Kushnir et al 1990). This difficulty can be overcome by scanning the cervix transvaginally, which provides clear cervical views without distortion. Several studies have viewed the cervix both in low risk pregnancies (Kushnir et al 1990, Zorzolli et al 1994) and pregnancies at high risk of a pre-term delivery (Iams et al 1994, Guzman et al 1994). Observation of the cervix prior to induction (i.e. as a comparison to the Bishop score) has been done in several studies (Paterson-Brown et al 1991, Boozarjomehri et al 1994). Investigations have shown the ultrasound measurement of the cervix to be objective and reproducible with little intra- or inter-observer error; (3.9 and 5.4% respectively; Zorzolli et al 1994) a marked distinction from the reports of digital cervical assessment, where interobserver differences of 20-30% have been reported (Stubbs et al 1986). Of those studies comparing transvaginal ultrasound (TVS) to digital assessment, both in terms of prediction of pre-term labour (Sonek et al 1990, Gomez et al 1994, Iams et al 1994) and prediction of ease of induction of labour (Boozarjomehri et al 1994), TVS was more sensitive and specific.

Cervical Incompetence and Transvaginal Ultrasound

Transvaginal ultrasound has also been used to investigate the clinical scenario of cervical incompetence; a diagnosis largely made on clinical grounds, with a history, often repeated, of late second trimester of early third trimester losses, following a rapid, relatively painless delivery, commonly of a live fetus in intact membranes. Diagnosis in a current pregnancy before advanced cervical dilatation and membranes bulging through the external os has proved difficult, with regular digital or speculum examinations providing little forewarning, and neither history nor examination helping with the prognosis in the present pregnancy (Barford and Rosen 1984). Measurement of the cervical compliance or resistance using hysteroscopy, cervical dilators or pressure transducers (van Duyl et al 1984, Zlatnik et al 1993), and measurement of a Cervical Resistance Index (Anthony et al 1982) have been described. This approach appears to compare favourably with a diagnosis of cervical incompetence based on the obstetric history (Anthony 1996), but does have the drawback of requiring instrumentation of the cervix, so largely precluding its use during pregnancy. In essence this means that physical assessment of cervical resistance will only be made in the non-pregnant state i.e. after a previous pregnancy loss suggestive of cervical incompetence.

Observation of the cervix using imaging techniques, largely ultrasound, has proved informative and potentially useful, but some interest has also been shown in magnetic resonance imaging (Hricak et al 1990). Imaging has the advantage over pressure or resistance measurements of the cervix in that it can be done during pregnancy without compromising cervical integrity and hence the fetus, and hence observation of cervical changes during pregnancy can be undertaken.

Several authors have suggested that cervical incompetence can be diagnosed or confirmed by the cervical appearance on ultrasound. Individual case reports (Joffe et al 1992) provided evidence of unusual cervical appearances associated with a history suggestive of cervical incompetence, whilst larger studies found a high incidence of abnormal cervical appearances on ultrasound in a group considered (on obstetric history) to be at risk of cervical incompetence (Michaels et al 1986). Further work (Guzman et al 1994) showed the possibility of demonstrating apparent cervical incompetence by applying pressure to the fundus of the uterus and observing changes in the cervix, particularly opening of the internal os, in response to the transmitted pressure.

Safety of Transvaginal Ultrasound

Definitive proof regarding the absence of an adverse outcome is essentially impossible to state with any certainty, but no research up to date has provided any evidence of a clinically harmful effect of transabdominal or transvaginal ultrasound in pregnancy. No increased incidence of fetal abnormalities have been published, and in particular there is the theoretical risk of increased chances of fetal harm from scanning in the first trimester during fetal development, but again there have been no reports of increased fetal abnormality with first trimester scans. The RADIUS study (Ewigman et al 1993) showed no difference in the incidence of IUGR in those randomised to routine ultrasound and those with ultrasound only used on clinical grounds. Looking further beyond pregnancy and delivery, three papers looking at childhood cancers and the in-utero exposure to ultrasound found no connection (Kinnier Wilson et al 1984, Cartwright RA et al 1984, Sorahan T et al 1995).

Several bodies have issued statements regarding the safety of ultrasound (RCOG Working Party 1984, European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) 1994, 1998, World Federation for Ultrasound in Medicine and Biology (WFUMB) 1997), the most recent (and most positive) being from the European Federation of Societies for Ultrasound in Medicine and Biology (1998):

"Based on scientific evidence of ultrasonically induced biological effects to date, there is no reason to withhold B- or M-mode scanning for any clinical application, including the routine clinical scanning of every woman during pregnancy."

No additional concern has been raised by the use of transvaginal rather than transabdominal ultrasound, although all bodies express caution with the use of ultrasound (and in particular Doppler waveforms, with the increased energy output involved) in the first trimester.

Table 1.1

Publications on Transvaginal scanning of the Cervix prior to 1996

Author	Date	Journal	Gestation of scans	Number of patients	Basis of publication
Brown et al	1986	Am J Obstet Gynecol	14-36 weeks	20	Comparison of TVS to abdominal approach
Ingermarsson et al	1989	Obstet Gynecol	Post EDD	103	Comparison of cervical score to spontaneous onset of labour
Andersen et al	1990	Am J Obstet Gynecol	8-30 weeks	178	Prediction of preterm delivery
Kushnir et al	1990	Am J Obstet Gynecol	8-37 weeks	166	Cervical length during pregnancy
Sonek et al	1990	Obstet Gynecol	All trimesters	83	Comparison of TVS to digital examinations
Paterson-Brown et al	1991	Eur J Obstet Gynecol Reprod Biol	Pre-induction	50	Comparison of TVS to Bishop score
Andersen	1991	J Clin Ultrasound		186	Comparison of TVS to abdominal ultrasound
Joffe et al	1992	Am J Obstet Gynecol		4	Cervical incompetence
Nzeh et al	1992	Int J Gynaecol Obstet	12-28 weeks	93	TVS of cervical incompetence
Smith et al	1992	J Ultrasound Med	9-37 weeks	109	Normal cervical values
Lim et al	1992	J Clin Ultrasound	37-42 weeks	81	Comparison of TVS to digital cervical assessment
Murakawa et al	1993	Obstet Gynecol	18-37 weeks	209	Normal cervical values
Guzman et al	1994	Obstet Gynecol	8-25 weeks	181	TVS and cervical incompetence
Iams et al	1994	Obstet Gynecol	24-35 weeks	60	TVS and threatened preterm labour
Boozarjomehri et al	1994	Am J Obstet Gynecol	Pre-induction	53	Cervical assessment and the ease of induction
Zorzolli et al	1994	Obstet Gynecol	12-31 weeks	154	Cervical change during pregnancy
Gomez et al	1994	Am J Obstet Gynecol	20-35 weeks	59	Comparison of TVS and digital cervical assessment in threatened preterm labour
Andersen et al	1994	Am J Obstet Gynecol	Post cerclage	32	TVS appearance following cervical cerclage and prediction of outcome
Iams et al	1995	Am J Obstet Gynecol	16-34 weeks	138	Cervical incompetence
Tongsong et al	1995	Obstet Gynecol	28-30 weeks	771	TVS as a predictor of a preterm delivery

Objectives of the MD thesis

As has been discussed, a great deal is known about the physiology of the cervix in pregnancy and labour, but the clinical appearances predictive value and importance of cervical changes in pregnancy are less well described. Transvaginal ultrasonography offers an opportunity to observe the cervix throughout pregnancy and provide details on the normal cervix in pregnancy, and also follow those considered at high risk of a pre-term delivery in view of their past obstetric history. The following investigations and results have been divided into separate chapters for elucidation and discussion. Chapter 2 involves volunteers studied in the first trimester of pregnancy, both those seen for reassurance scans and also those with a threatened miscarriage. Chapter 3 looks at the women in the control population in the second and third trimesters i.e. women at low risk of a pre-term delivery, both nulliparous women and multiparous women with previous full term deliveries. Chapter 4 relates to those women studied who were considered at high risk of a preterm labour, mainly due to a history of a previous second trimester loss or a preterm delivery, and in particular comparison of the results between the high risk and low risk groups will be discussed. Of significant interest, equivalent to the study by Guzman et al (1997) are those individuals within the high risk group in whom cervical changes were noted in response to fundal pressure; a separate chapter (Chapter 5) will be devoted to this small group within the high risk cohort. Chapter 6 concerns the cervical appearance of those women offered induction of labour for prolonged pregnancy (over 41 weeks gestation).

Chapter 2

Methods and Materials

Recruitment

All women involved in this research were booked for delivery at Southmead Hospital in Bristol. Prior to any recruitment being undertaken, the hospital consultant staff, the Antenatal Clinic midwifery staff were written to regarding the study and comments and suggestions requested. Ethical committee approval for the research was obtained from both Southmead and Frenchay Ethics Committees prior to recruitment. Information sheets were sent to community midwives and GPs of each patient recruited to the study.

For the second and third trimester recruitment, posters were displayed around the Antenatal Clinic, asking for volunteers to take part in the study, either as high risk or low risk candidates. Information leaflets were available for those who expressed an interest, or in particular those who were identified as high risk of a preterm delivery by the Antenatal Clinic staff or medical staff, were referred to me to discuss whether they would wish to be involved in the research. Those who agreed to be involved were allocated to the high or low risk categories depending on their past obstetric history and risk factors in the present pregnancy (Table 2.1). Those who declined to take part were not follow up as part of the study. All women recruited to the study signed a written consent form prior to inclusion in the study.

'Low risk' was defined as having none of the risk factors commonly associated with an increased risk of a pre-term delivery, adapted from Holbrook et al (1989) - Table 2.1. High risk pregnancies were defined as those having one or more major risk factors, or two or more minor risk factors.

Table 2.1

Criteria for dividing into High or Low risk Pregnancies (Chapters 4 and 5)

1 major or 2 minor risk factors required for inclusion into the High Risk group. All others classed as Low Risk.

Major Risk Factors	Minor Risk Factors
Previous preterm delivery Previous second trimester loss	Cigarette smoking (>10 per day) Vaginal bleeding in index pregnancy after 12 weeks gestation Age under 20 Three of more terminations of pregnancy

First trimester recruitment (Chapter 3) was done from the Early Pregnancy Clinic run daily in the Cotswold Centre. The clinic patients were referred by their GP or community midwife with either a threatened miscarriage or for reassurance due to a past pregnancy loss (miscarriage or ectopic pregnancy). All scans to confirm viability were performed transvaginally by the Southmead Hospital

Radiographers. Prior to scanning all women were asked if they would agree to a continuation of the viability scan to view the cervix if the pregnancy was found to be viable (or unconfirmed due to it being too early). Those that agreed and had a viable pregnancy were then scanned at the same visit by the author. All women in the first trimester scans were only scanned once.

For the study investigating cervical measurements at induction of labour, women were approached on the antenatal wards prior to the induction of labour. Those that agreed to take part in the study were scanned prior to induction of labour, with each woman being scanned only once.

Ultrasonography

All scans were performed by the author on an Ultramark 4-Plus ultrasound scanner located in the Cotswold Centre for Women's Health in Southmead Hospital. The basis for the method of transvaginal scanning was described in detail by Iams et al in 1995, with the application of fundal pressure first being described by Guzman et al (1994). The reproducibility of the scans was demonstrated by a small study performed following the completion of the main research to measure the degree of intra-observer error in my method of transvaginal measurement of the cervix.

Intra-Observer Error Study

A total of ten patients were scanned between April and July 2000 at Bath Royal United Hospital with the aim identifying the intra-observer error. All were scanned by the author in the Bath antenatal clinic and all had had a previous preterm delivery as the clinical indication for a transvaginal scan of the cervix. The scans were all done with verbal patient consent.

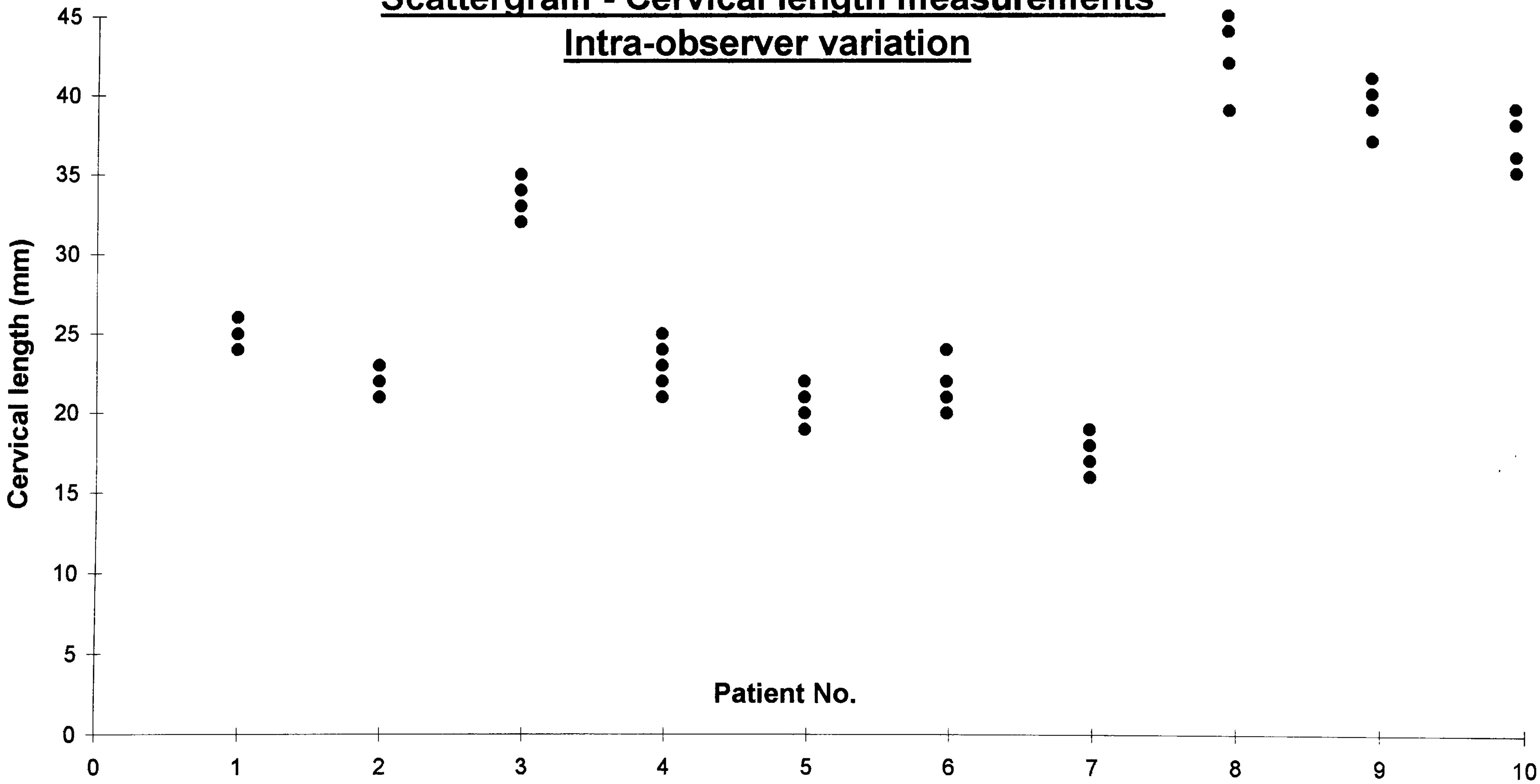
Scans were performed on an ATL ultrasound machine with a 5 Mhz transvaginal probe covered with a condom for sterility. All women had an empty bladder and five measurements were taken of the cervical length (internal to external os). The measurements were recorded by a third party, independently of the author.

Results

The median cervical length of the ten patients in this study was 24 mm (range 17.4 - 39.2 mm), over a gestational age range of 18-35 weeks. The median variation of measured cervical length from the mean for each individual was 6.6% (range 4 - 12.1%; 1 - 2.6 mm) - Figure 2.1.

These results are in line with published intra-observer errors (Zorzolli et al 1992, Heath et al 1998).

Figure 2.1
Scattergram - Cervical length measurements
Intra-observer variation



Transvaginal scan

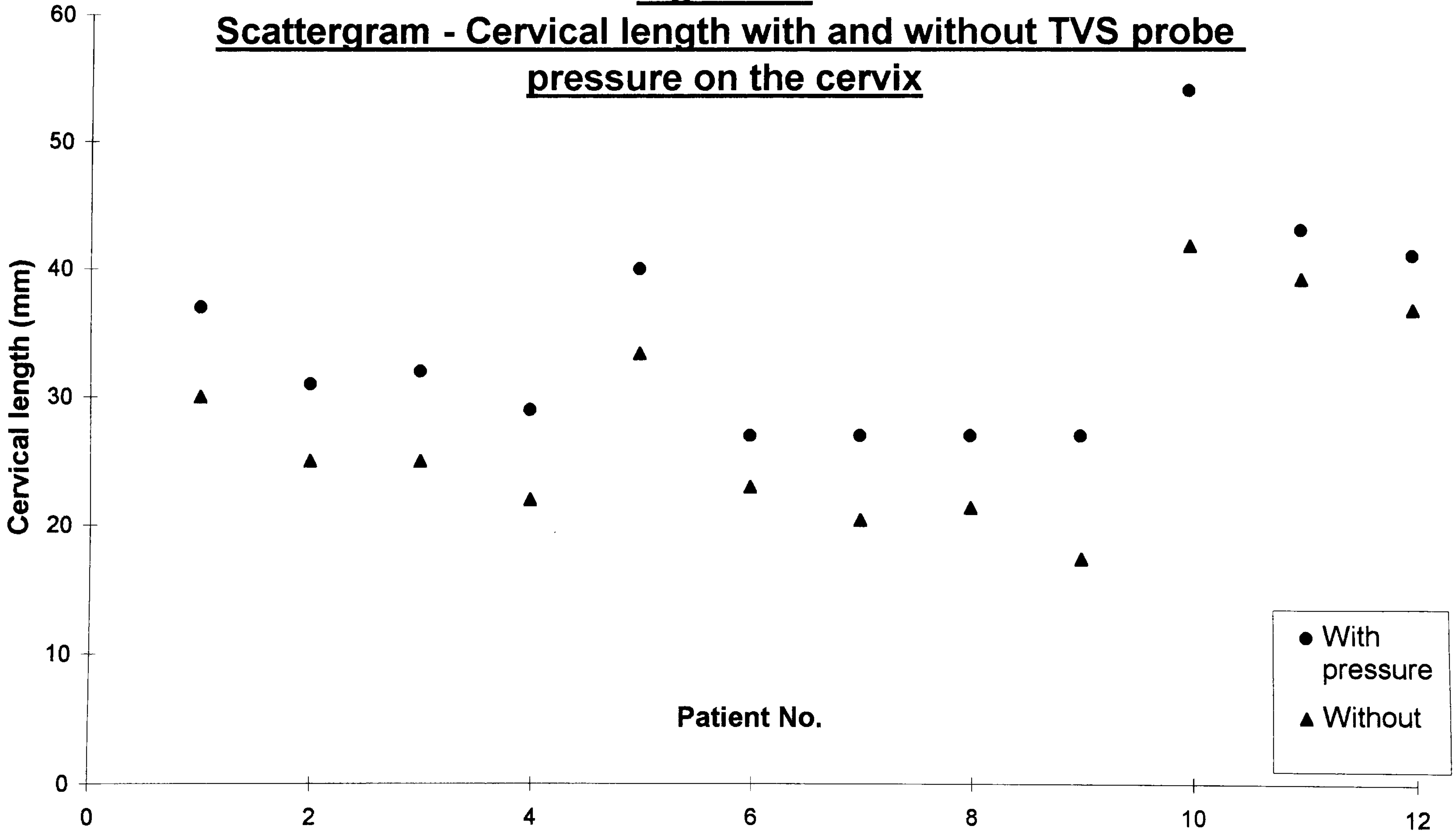
After ensuring the woman had an empty urinary bladder, a 5.0 MHz transvaginal probe was covered with a condom, lubricated with sonor lucent jelly and inserted into the vagina. For ease of movement of the probe the woman was lain prone with her pelvis raised off the bed on a cushion or pillow. The cervix was identified and the internal and external os visualised. Once the length of the cervical canal could be clearly seen as a continuous white line from internal to external os, the transvaginal probe was withdrawn to ensure no distortion or elongation of the cervix which can be caused by the transvaginal probe itself. Cervical measurements were taken at the point where clear visualisation of the cervix was still possible, but when there was no pressure from the probe on the cervix (Fig. 4.1), as first described by Iams et al (1995).

Study into variation of cervical length with TVS probe pressure

A study done to demonstrate the elongation of the measured cervical length caused by transvaginal probe pressure was undertaken following the completion of the initial research. Twelve patients, scanned because of previous preterm deliveries, were scanned at Bath Royal United Hospital between April and July 2000. Measurements were taken of the cervix with pressure on the cervix with the TVS probe and without. The results are shown in Figure 2.2.

Figure 2.2

Scattergram - Cervical length with and without TVS probe pressure on the cervix



The median difference in cervical length with pressure from the TVS probe was 6.6 mm (range 3.8 - 12.2 mm). In terms of a proportion of the cervical length this translates to between 11.4% and 55.2% of the resting cervical length (median percentage change 27.9%); sufficient to make a material difference to the measurements, and showing the importance of avoiding pressure on the cervix with the TVS probe whilst taking cervical measurements.

In the first trimester, clear demarcation of the internal os was often difficult due to a lack of separation of the lower uterine segment at this early gestation. The position of the internal os was taken as the start of the echo-poor "halo" around the intra-uterine gestation sac (Fig 3.1). If the whole canal could not be visualised complete (usually due to a sharply retroverted uterus) then the procedure was abandoned.

Three measurements were taken of the cervix; cervical length, cervical width and any opening ("beaking") of the internal cervical os. In view of the degree of cervical distortion caused by the vaginal probe pressure on the cervix demonstrated above, the smallest cervical width and cervical length were taken as the most reproducible and accurate measurements. Cervical length was defined as the maximum length of closed cervical canal, measured from the external os up to where the amniotic fluid was visible. Cervical width was measured at the level of the maternal bladder at right angles to the cervical canal, whilst beaking of the cervix was defined as the maximum width at the level of the internal os (at right angles to the cervical canal) of any opening of the cervical canal. The measurements were then repeated following a short period of sustained manual pressure on the uterus, in particular looking for any cervical shortening or opening of the internal os. Guzman et al (1994) initially described this approach using pressure on the uterine fundus. In many women, particularly the more obese patients, I found more effective pressure could be applied pressing suprapubically on the uterus, hence both fundal and suprapubic pressure was applied, and the largest cervical changes noted were recorded.

Transabdominal scan

In the second and third trimester, an abdominal scan of the fetus was also performed, looking at fetal growth (fetal head circumference and fetal abdominal circumference), liquor volume and placental site. The abdominal scan was performed both as a screening procedure for fetal growth and also for maternal reassurance to encourage interest in the study.

Statistical Methods

All statistical calculations were done using SPSS Statistical package, standard version (1995). Assistance with the appropriate statistical methods to use was obtained from Mr Chris Foy, Statistician with the Gloucestershire Health Authority.

All outcome variables were tested for normality prior to any statistical measures. Those that were found to have a normal distribution using the 1-sample Kolmogorov-Smirnoff test (e.g. gestation at delivery in the low risk group (Chapter 4), or cervical length or width at all gestations) then the test used to look for differences between two groups was the unpaired t-test. Throughout a p value of <0.05 was considered statistically significant. The Bonferroni correction (where the corrected p-value = p x k, where k is the number of different t-tests derived from the same data) was used in Chapters 4 and 5 with regard to cervical length and possible associations. The resulting p-value is undoubtedly conservative but does reduce the risk of a false positive result.

The "normograms" in Chapter 4 (Figures 4.3, 4.4 and 4.5) were derived from the cervical measurements of all women in the low risk group. A single measure from each of the 51 women in the low risk group was included in each time frame (e.g. 18-20 weeks), and the mean calculated from these values. The 5th and 95th centiles were used rather than 2 standard deviations from the mean due to the small sample size; the use of standard deviations implies a normal distribution of the data (which is more difficult to state with confidence with a small sample size) and also the use of standard deviations is more likely to lessen the importance of the extreme values than centiles, particularly with a small sample size.

In Chapter 4 and 5, stepwise multiple linear regression analysis was used to assess the possible effect of all measured variables on both cervical length and also gestation at delivery. As has already been stated, cervical length and gestation at delivery in the low risk group were normally distributed, so allowing a regression analysis on the raw data. In the high risk group, the gestation at delivery was not normally distributed, with a large negative skew in view of the significant numbers of preterm deliveries. This difficulty was overcome by converting the gestation at delivery into week prior to 42 weeks gestation when delivery occurred (e.g. a delivery at 32 weeks was +10), and then taking the $\log_e$ of the transformed data, so producing a normally distributed data set, which then could be used in the multiple linear regression analysis as with the low risk data.

Non normally distributed data, such as the gestation at delivery in the first trimester group (Chapter 3) were compared to cervical length or width using a non-parametric method; the Mann Whitney U Test.

Calculation of the power of the studies (e.g. the comparison of elective to emergency cerclage, Chapter 5) was done with reference to the normogram devised by Altman (1982).

Chapter 3

The Cervix in Early Pregnancy; an assessment of first trimester cervical measurements on transvaginal ultrasound with regard to outcome

Introduction

The cervix and cervical length have been extensively studied in the second and third trimesters, but there has been little published research into the cervical appearance in the first trimester. Zorzolli et al in 1994 published results looking at 154 women (of whom 3% had had a previous preterm delivery) followed though the second and early third trimesters, with the first scan being performed at 12 weeks gestation. The mean cervical length measured at this gestation was 43 mm. As part of a larger study looking at the cervix throughout pregnancy, Kushnir et al (1990) scanned 48 women between 8 and 13 weeks gestation, with a mean cervical length in this group of 43 mm. All were considered at a low risk for a preterm delivery. Guzman et al (1994) reported on a series of women with a previous history of cervical incompetence, in which it is stated that the earliest scans were performed at 8 weeks gestation, but no specific details of the first trimester scans were published. No publications have investigated the cervix prior to 8 weeks gestation.

15-20% of all pregnancies end with miscarriage in the first trimester, and approximately 50% of these are associated with a chromosomal or structural fetal abnormality (Howie 1995, Edmonds 1997). Uterine abnormalities and immunological factors may also play some part in a proportion of cases of miscarriage, but in a significant proportion of first trimester losses no clear cause is found. As the cervix is considered one of the potential causes of a late (second trimester) miscarriage, it would appear worthwhile investigating the cervix in the first trimester, and determine whether the first trimester cervical measurements correlate to pregnancy outcome.

Study Design

Southmead Hospital has an Early Pregnancy Clinic, at which women can be seen, at the request of their GP or midwife, for an ultrasound scan and assessment. The majority are referred for problems such as bleeding in early pregnancy, pelvic pain or for reassurance following a previous pregnancy loss. Most women present at 5-8 weeks gestation, at which time it can be difficult to confirm fetal viability with trans abdominal scanning. The majority of women are therefore offered a transvaginal scan in order to obtain a definitive diagnosis. All women are reassured at the time of the scan that ultrasound is felt safe in pregnancy (RCOG Working Party on Routine Ultrasound Examination in Pregnancy 1984) and also the insertion of a vaginal probe carries no risk of causing a miscarriage. For the majority of women a transvaginal scan is only mildly uncomfortable, and visualising the cervix contributes no additional pain. All woman undergoing a transvaginal scan in the Early Pregnancy Clinic in whom a viable intra-uterine pregnancy was found were asked for consent to measure the cervix at the same time. The fetal viability scans were performed by the Southmead

Hospital radiographers with specific training in transvaginal scanning; all the cervical measurements were performed by the author.

Method

The method of scanning has been described in Chapter 2. The outcome of the pregnancies was determined from the hospital computer records of pregnancies and deliveries, and outcome was compared to the first trimester scan data collected.

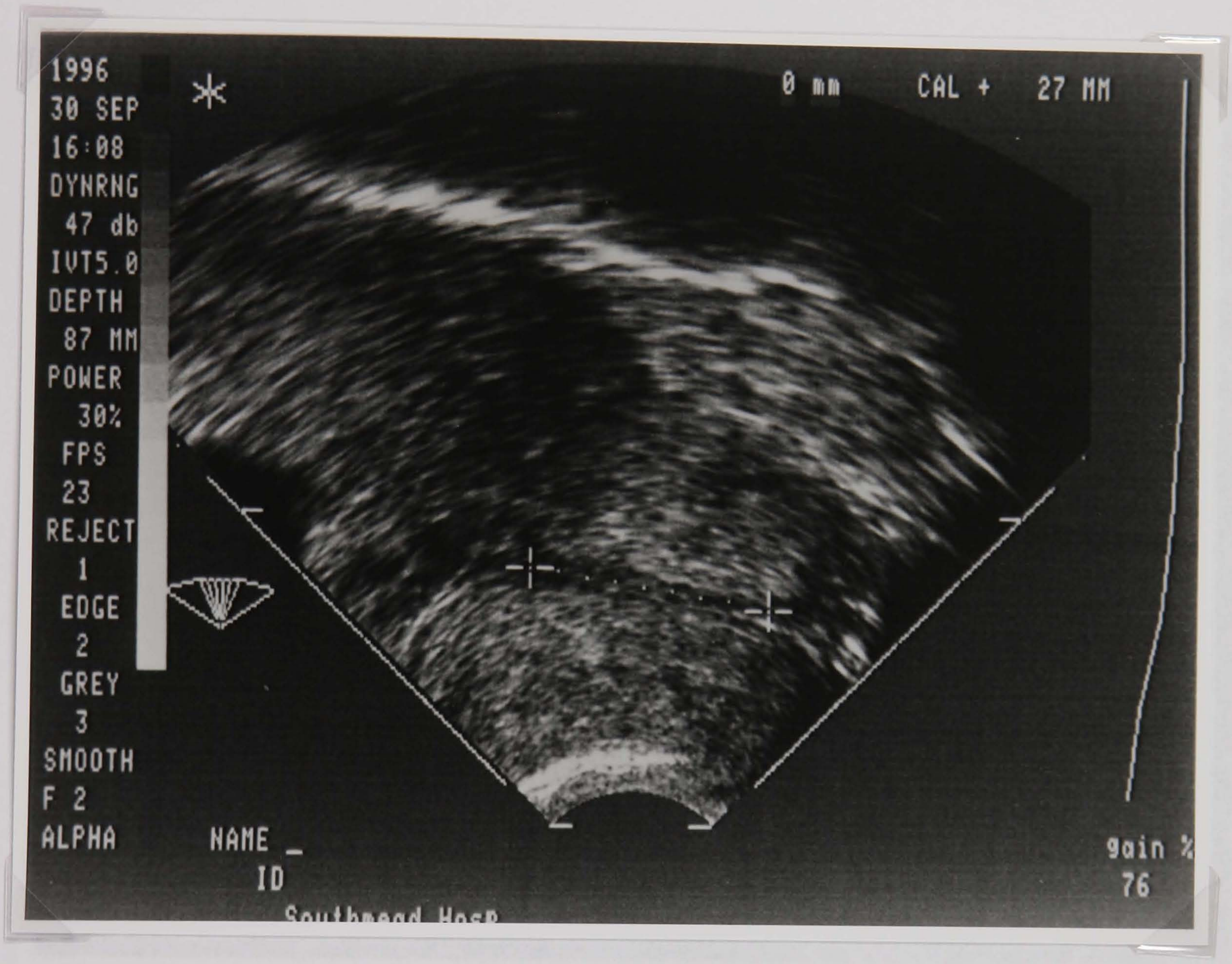


Figure 3.1

Transvaginal ultrasound view of a normal cervix at 12 weeks gestation. The cervical length (+-----+) is 27 mm, but the position of the internal os is indistinct due to the placenta being low in the uterine cavity, and also the fact that, at this stage of pregnancy, the lower segment is commonly not filled with the amniotic sac and hence the anterior and posterior walls are not separated.

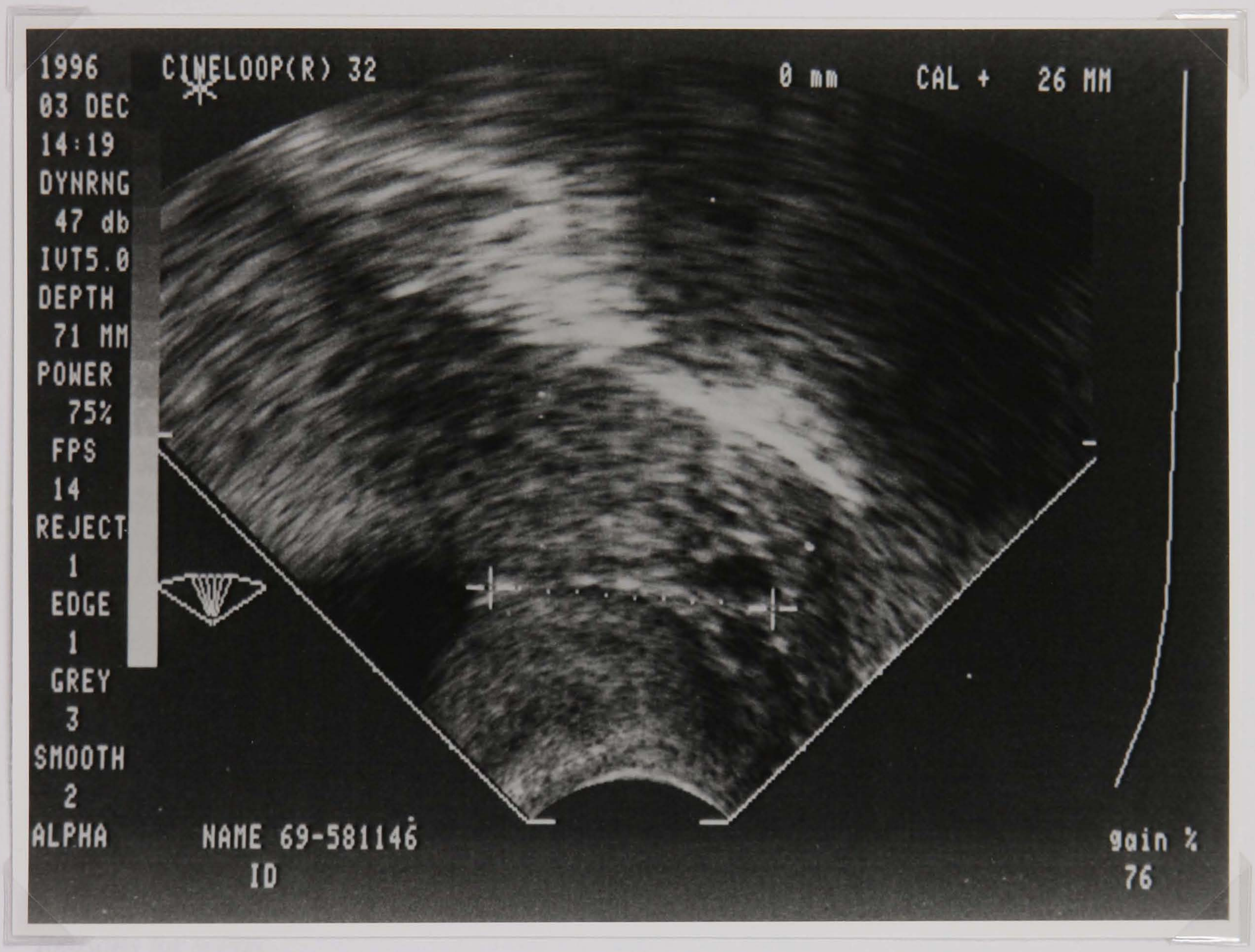


Figure 3.2

Transvaginal ultrasound picture of the same cervix in 3.1, but at 18 weeks gestation. The placenta is no longer covering the internal os, and the lower segment has opened up further, providing a far clearer view of the position of the internal os.

Setting

The Cotswold Centre for Women's Health, Southmead Hospital

Study duration

November 1996 - March 1997

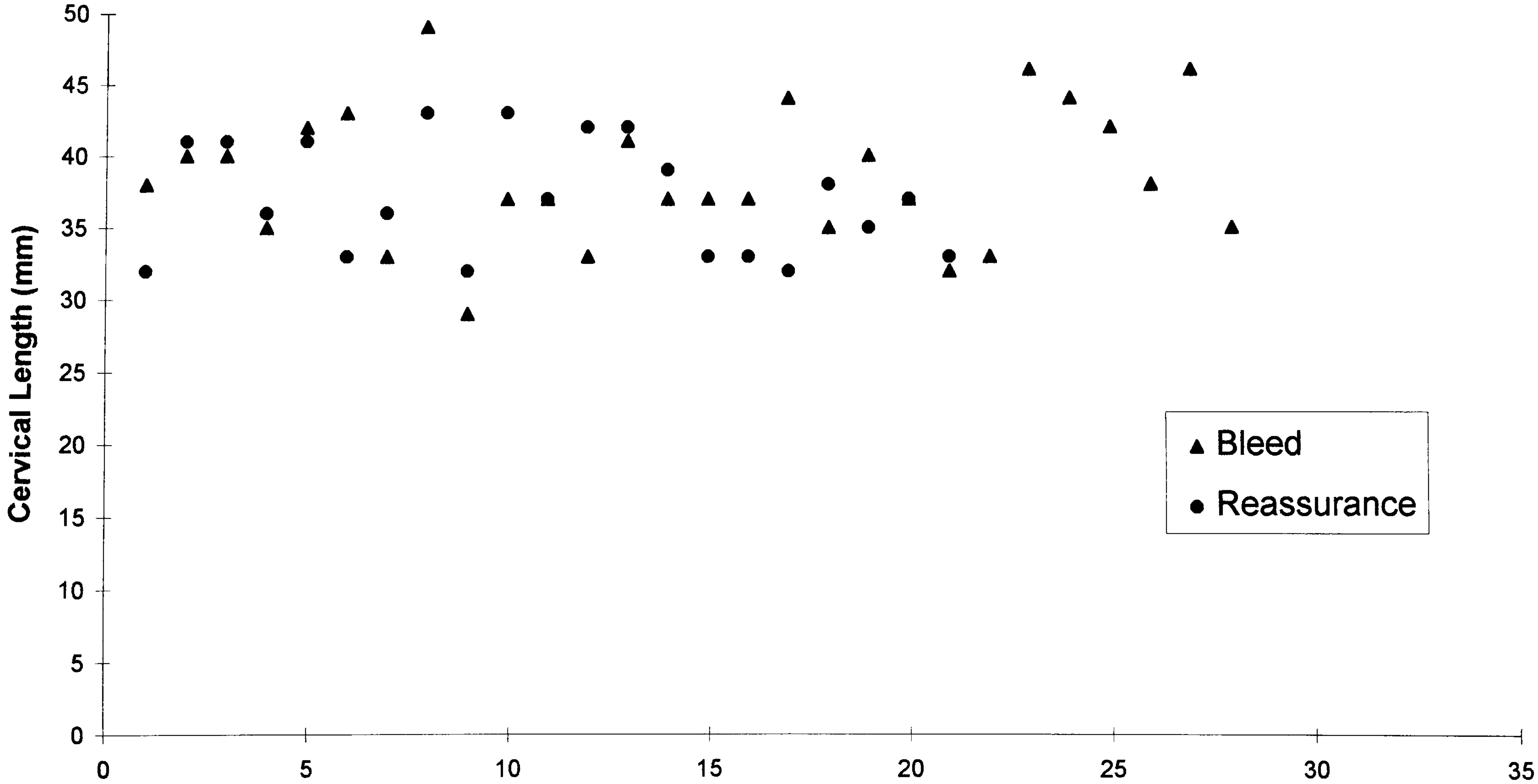
Results

A total of 68 women were scanned in the first trimester, with a gestational range of 4 to 12 weeks (mean = 6.6; median = 6; sd = 1.36). In 10 scans (14.7% of all scans performed) a clear view of the entire cervical canal was impossible, largely due to a sharply retroverted uterus. Twelve scans were not definitive regarding fetal viability initially and subsequently ten were shown to be either a missed or incomplete miscarriage. Hence the results from a total of 48 scans of viable first trimester pregnancies can be reported, with the non viable results being considered separately.

Reasons for scans

The reasons for the early pregnancy scan were bleeding (n = 36), pelvic pain (n = 1) or reassurance due to a previous ectopic or first trimester miscarriage (n = 21) - Figure 3.3. Of those found to have a non-viable pregnancy (n = 10) eight were seen because of vaginal bleeding.

Figure 3.3
Scattergram of First Trimester Cervical Lengths



Cervical Measurements

In those with a viable pregnancy, the average cervical length was 37.9 mm (sd = 4.5), whilst the average cervical width was 30.2 mm (sd = 4.1). None of the cervices measured at this stage of pregnancy had any measurable beaking at rest or in response to fundal pressure. A comparison in the viable pregnancies between those scanned for reassurance and those with a threatened miscarriage (bleeding in early pregnancy) showed no statistical difference between the mean cervical lengths or widths in the two groups (Table 3.1). Equally, considering those with a non-viable pregnancy (n = 10), there was no statistical difference in cervical length or width between the viable and non-viable pregnancies (Table 3.2).

Table 3.1

Comparison between scans for reassurance and first trimester bleeding (viable pregnancies)

	Cervical Length mean (sd)	**Cervical Width mean (sd)**
Reassurance scans n = 20	37.1 mm (4.0)	30.6 mm (3.6)
First trimester bleeding n = 28	38.4 mm (4.67)	30.0 mm (4.66)
Unpaired t test	t = 1.05 p = 0.31	t = 0.50 p = 0.63

Table 3.2

Comparison between viable and non-viable first trimester scans

	Cervical Length mean (sd)	**Cervical Width mean (sd)**
Viable pregnancies n = 48	37.8 mm (4.39)	30.2 mm (4.16)
Non-viable pregnancies n = 10	37.1 mm (8.16)	29.4 mm (3.53)
Unpaired t test	t = 0.28 p = 0.79	t = 0.60 p = 0.55

Gestation at delivery.

Of the 48 women seen with a confirmed viable intrauterine pregnancy, one (2%) subsequently miscarried. Two others decided to go for a termination of pregnancy at the end of the first trimester, and in a further three no record of the pregnancy outcome could be found, either due to records being lost or their decision to deliver at a different hospital. Hence in total demographic data was available on all 48 women, but only a total of 42 women had a known gestation of delivery in the third trimester.

A comparison between those women scanned for a threatened miscarriage and those scanned for reassurance, showed a median gestation of delivery in those scanned because of a first trimester bleed of 37.5 weeks (range 20-41 weeks), and 37.0 weeks (range 32-41 weeks) in those scanned for reassurance. As the gestation at delivery was not normally distributed, a comparison between the two groups was done using a Mann Whitney U test: this showed no difference in gestation at delivery between the two groups ($p = 0.359$).

Prediction of pre-term delivery

Of the 48 with a viable first trimester scan, five (10%) delivered preterm (mean = 31.8 weeks, median = 35.5, sd = 7.85, range 20-36 weeks). Neither cervical length nor cervical width were normally distributed, so a Mann-Whitney U test was used to compare both past history and cervical measurements between those with a term and those with a preterm delivery. There was no significant difference between the two groups in terms of pre-pregnancy risk factors (smoking, number of previous terminations, parity or number of previous preterm deliveries), and there was also no difference in the preterm delivery rate between these two cohorts (Table 3.3). There appears to be a large difference between the two groups (preterm and term) in terms of the mean ranks in the Mann-Whitney U test, so the data were compared to gestation at delivery as a continuous variable, after transformation of the gestation data into the $\log_e$ of time from 42 weeks gestation to make it normally distributed (see Chapter 2 - Statistical Methods). This also showed no correlation between gestation at delivery and cervical length or width in the first trimester of pregnancy.

Table 3.3
First trimester scans and gestation at delivery

Mann Whitney U Test

	Cervical Length mean rank	**Cervical Length sum of ranks**	**Cervical Width mean rank**	**Cervical Width sum of ranks**
Term Delivery n = 37	22.27	824	21.34	747
Preterm Delivery n = 5	15.8	79	14.60	73
p values	p = 0.27		p = 0.23	

Discussion

Cervical measurements in the first trimester is straightforward to perform. A failure rate of 14.7% corresponds approximately to the accepted incidence of a retroverted uterus of 20% (Vellacott 1997); such a problem is of no concern in the second and third trimesters, when the retroverted uterus has lifted out of the pelvis.

A comparison with previous studies (Kushnir et al 1990, Zorzolli et al 1994) is difficult, as no report of cervical measurements prior to 8 weeks has been reported. However, both Kushnir (at 8-13 weeks) and Zorzolli (at 12 weeks gestation) reported an average cervical length in early pregnancy of 43 mm, somewhat longer than our average of 38 mm for all measurements between 5 and 12 weeks gestation.

Beaking or funneling of the internal cervical os was not found in our population in the first trimester. As this is strongly associated with pre-term labour and the suggestion of cervical incompetence (Joffe et al 1992, Fox et al 1996, Guzman et al 1997) we can tentatively suggest that this might only be a second or third trimester phenomenon. The results from this study have demonstrated no benefit in first trimester scanning in the prediction of either a pre-term delivery or a first trimester pregnancy loss, but a larger study may well have the power to show a statistically significant result. The present data shows a mean cervical length of those delivering preterm in 33.4 mm, whilst the mean cervical length in those with a term delivery is 38.4 mm, with a standard deviation for all cervical lengths of 4.39. If these differences were replicated in any future trial, a power of 80% and a p value of 0.05 would only require a sample size of 28 to demonstrate a statistically significant difference in cervical lengths between those delivering at term and those delivering preterm (Altman 1982). Considering the small sample size, no real conclusions can be drawn from this pilot study, other than the notable absence, in this group, of any funneling or beaking of the internal cervical os.

Subsequent Publications

Since the start of this research in 1995, only one paper has been published looking specifically at cervical length measured on TVS in the first trimester (Zalar 1998).The results of 373 scans of women at about 11 weeks gestation were reported as showing an association between a shorter cervical length in the first trimester and early delivery. However, the results were not clear cut. The 10th centile of cervical length was quoted as 40 mm, a length later in pregnancy closer to the 50th centile in other studies, and a measure also at variance with the results from my study of a average cervical length in the first trimester of 38 mm. Secondly, the most significant association described was between a short cervical length and history of preterm prelabour, a clinical diagnosis with an acknowledged high false positive and false negative rate (Kragt and Kierse 1990, O'Driscoll 1977, Turnbull 1989). The association was then drawn between those with a history of preterm prelabour and early delivery, rather than with a short cervix in the first trimester. Also the gestation difference at delivery, although statistically significant is not of any real clinical significance (38.7 weeks compared to 39.9 weeks).

This publication, with larger numbers than we were able to recruit in Southmead, provides more useful information than we were able to produce with a small study. However I do not feel it provides the definitive answer regarding first trimester scans and the potential association between cervical length in the first trimester and gestation at delivery. Further work is needed.

Chapter 4

Transvaginal Ultrasound Assessment of the Cervix in the Second and Third Trimesters in Pregnancies at Low Risk of Preterm Labour

Introduction

Cervical assessment by digital vaginal examination is both subjective (Stubbs et al 1986) and limited in its value; predictions of preterm labour based on contractions and vaginal assessment of the cervix has an accuracy of only 30-80% (Kragt and Kierse 1990, O'Driscoll 1977, Turnbull 1989). Investigation has hence been directed elsewhere in an effort to obtain an accurate picture of the cervix during pregnancy. Observational studies using transvaginal ultrasound to monitor the cervix in women at low risk of a preterm delivery has been published in the past (Zorzolli et al 1994, Murakawa et al 1993, Kushnir et al 1990) but most investigated a low risk population only, with no associated high risk population for comparison. I drew high risk and low risk cohorts from the same population with the measurements performed by a single operator on a single ultrasound machine in order to have meaningful comparisons between high and low risk cohorts.

The use of transvaginal ultrasound allows clear visualisation of the cervix and accurate measurements of the cervical dimensions (Fig. 4.1).

Figure 4.1

Transvaginal ultrasound image of a normal cervix at 30 weeks

The fetal head is to the left, with the calipers +------+ showing the positions of the internal and external os. The cervical length is 35 mm.

Studies have published normal values for the cervix (in particular cervical length), with an average cervical length varying both from study to study and with gestation. Normal cervical length measurements varied from 35 mm (Iams et al 1996) to 48 mm (Kushnir et al 1990), whilst changes with gestation described included a significant shortening of the cervical length from 20-25 weeks to 32-37 weeks (Kushnir et al 1990) and a change in cervical shape from cylindrical to conical over time (Zorzolli et al 1994). The aim of this study was to observe the normal cervical appearance in a population at low risk of preterm labour.

Method

The entry into the study and the ultrasound scanning method has been described in Chapter 2.

Those fitting the criteria (Table 2.1) were enrolled into the study. Each woman was seen approximately every 3 weeks from enrollment up to at least 33 weeks, with further scans beyond this gestation if the women wished to continue. Each visit involved both transvaginal and transabdominal scans.

Setting

All scans were performed in the Cotswold Centre for Women's Health, Southmead Hospital on an Ultramark 4-Plus ultrasound scanner, using a 5.0MHz transvaginal probe, and a 3.5MHz linear sector transabdominal transducer.

Study Duration

January 1996 - July 1997

Results

Demographics

A total of 51 women were enrolled into the low risk group. The average age at conception was 27.9 years. Twenty women (39%) were primiparous, whilst 31 (61%) had had one or more previous term deliveries. A total of 13 women had previously had terminations of pregnancy, with two having undergone three terminations of pregnancy, two having had two previous terminations, and the remaining nine having had just one termination of pregnancy each. None had had a prior preterm delivery, and none had had a spontaneous late second trimester miscarriage (three women had undergone an induced termination in the second trimester). 16% of the low risk group smoked 10 or more cigarettes per day.

Pregnancy Outcome

Gestation at delivery

There were no second trimester losses in this low risk group, and just one pre-term delivery at 36 weeks gestation (2%). The mean gestation at delivery was 39.4 weeks (median 39.5, range 36-42 weeks). The modes of delivery are shown in Table 4.1.

Table 4.1

Delivery Details - Low Risk Population

Type of delivery	Number in low risk group (%)
Normal vaginal delivery	36 (70.6)
Elective Caesarean section	6 (11.8)
Emergency Caesarean section	4 (7.8)
Ventouse Delivery	2 (3.9)
Forceps Delivery	2 (3.9)

Birthweight

Birthweight data was available on 50 of the 51 women (one moved away from the area at term prior to delivery). The mean birthweight in this 50 was 3.35 kg (range 1.67-4.50 kg).

Cervical Data

Several approaches to the cervical data will be presented. Presentation of the data as a whole, showing cervical change with gestation, demonstrates the expected "normal" values from a low risk population. Comparison of primiparous with multiparous women is of relevance, as well as between those with or without a history of termination of pregnancy or previous miscarriages. Comparisons between the high and low risk groups will be discussed in more detail in Chapter 5.

Normal Cervical Values

On outcome as well as intent, this is a low risk group; the average gestation at delivery was 39.4 weeks, with just one delivery prior to term (at 36 weeks); a 2% preterm delivery rate. Figure 4.2 shows a scattergram of the cervical lengths at the first visit, whilst Figure 4.3 shows a "normogram" of the cervical lengths obtained from this group at each gestation. From the end of the second trimester to term, the average cervical length falls by 53%, from 39.9 mm to 18.7 mm. Figure 4.4 shows the cervical widths at each gestation, and in contrast to the cervical length, little change in cervical width over time is demonstrated. The percentage change is only 20%, from 38.7 mm to 49 mm. No normal values for cervical "beaking" (opening of the internal os) have previously been published, despite its being considered an indicator of preterm labour or cervical weakness (Fox et al 1996). Figure 4.5 shows the normal values from this population. Although there is a wide variation in values at all gestations, there is still almost a fivefold increase in the mean opening of the internal os from 18-20 weeks up to term (1.5 mm to 7.3 mm). All these cervical changes are statistically significant over the timescale from first measurement to the end of the third trimester (t values of 6.45, 4.48, 4.79 respectively, all $p < 0.001$).

Figure 4.2
Scattergram of First Visit Cervical Lengths
Low Risk Group

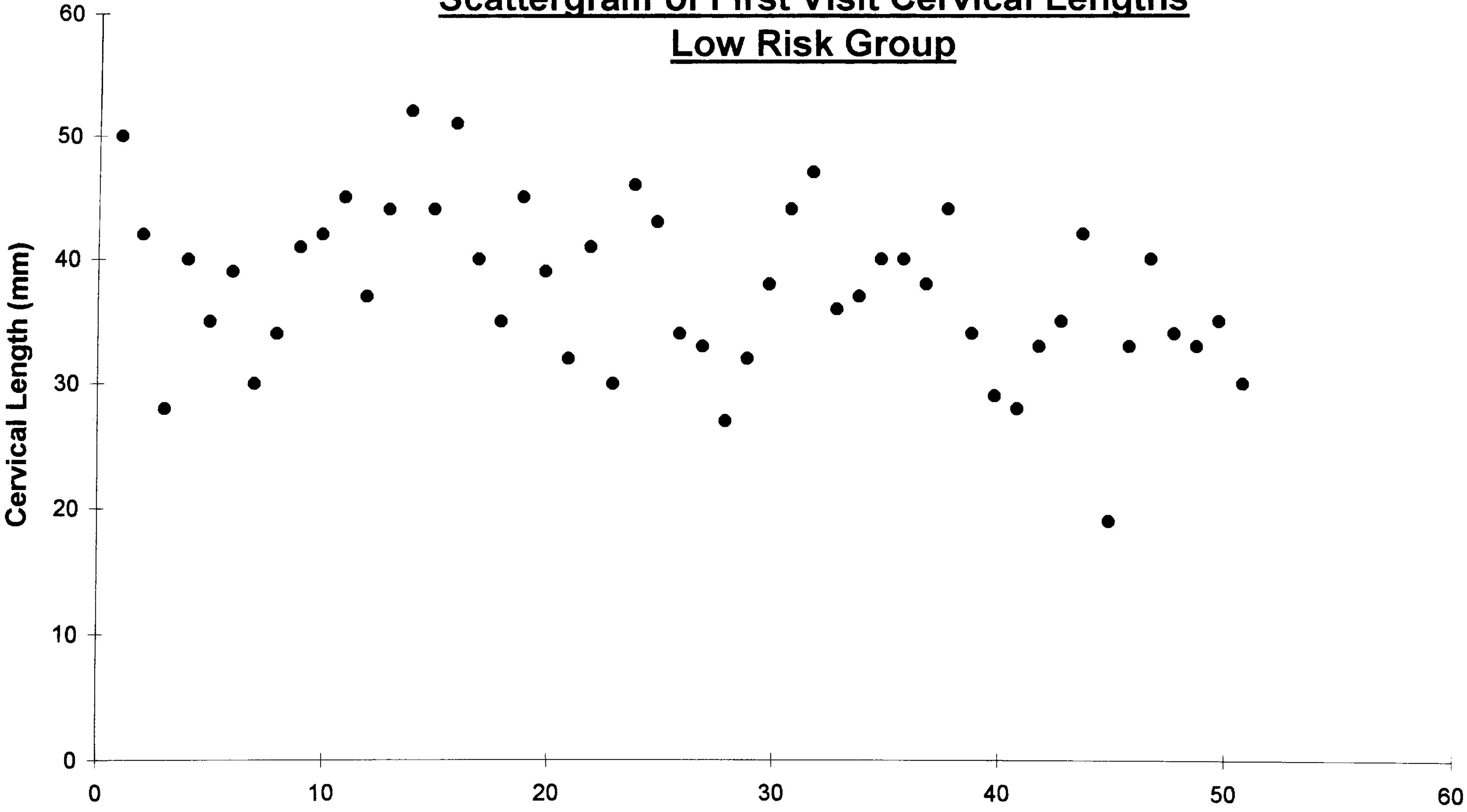


Figure 4.3 - Cervical length in Low Risk population (mean +/- 5th-95th centiles)

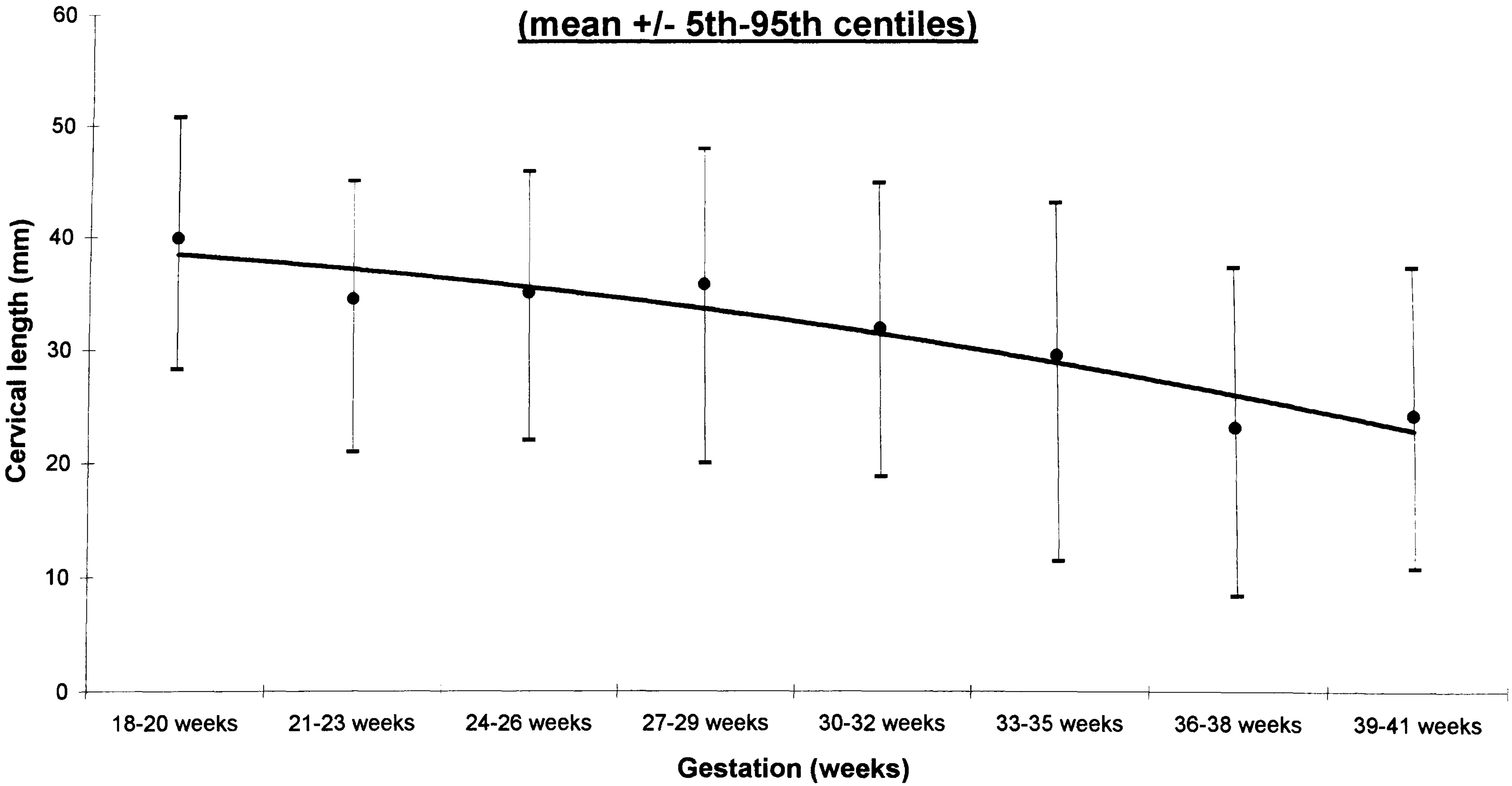


Figure 4.4 - Cervical width in Low Risk population (mean +/- 5th-95th centiles)

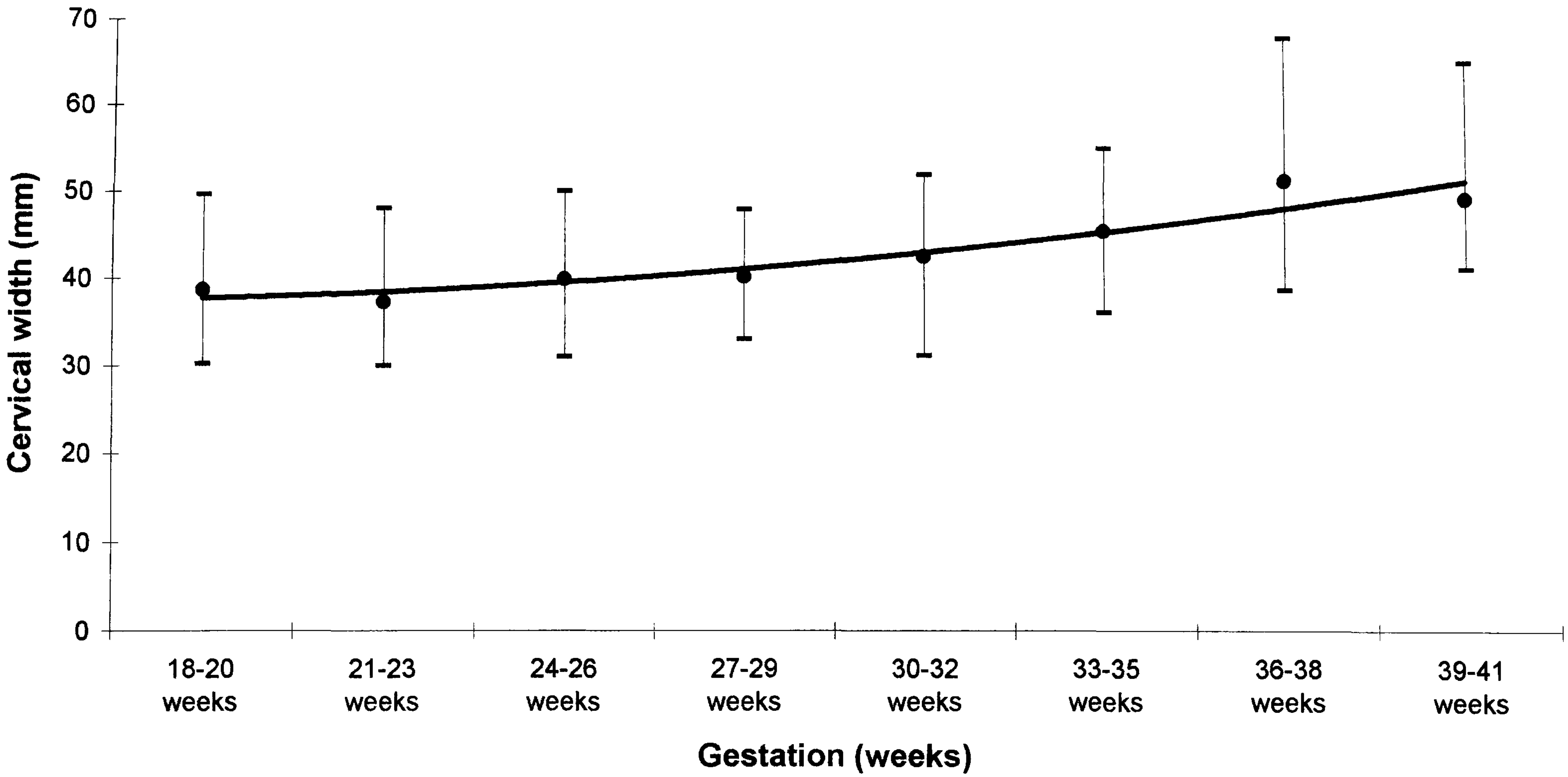
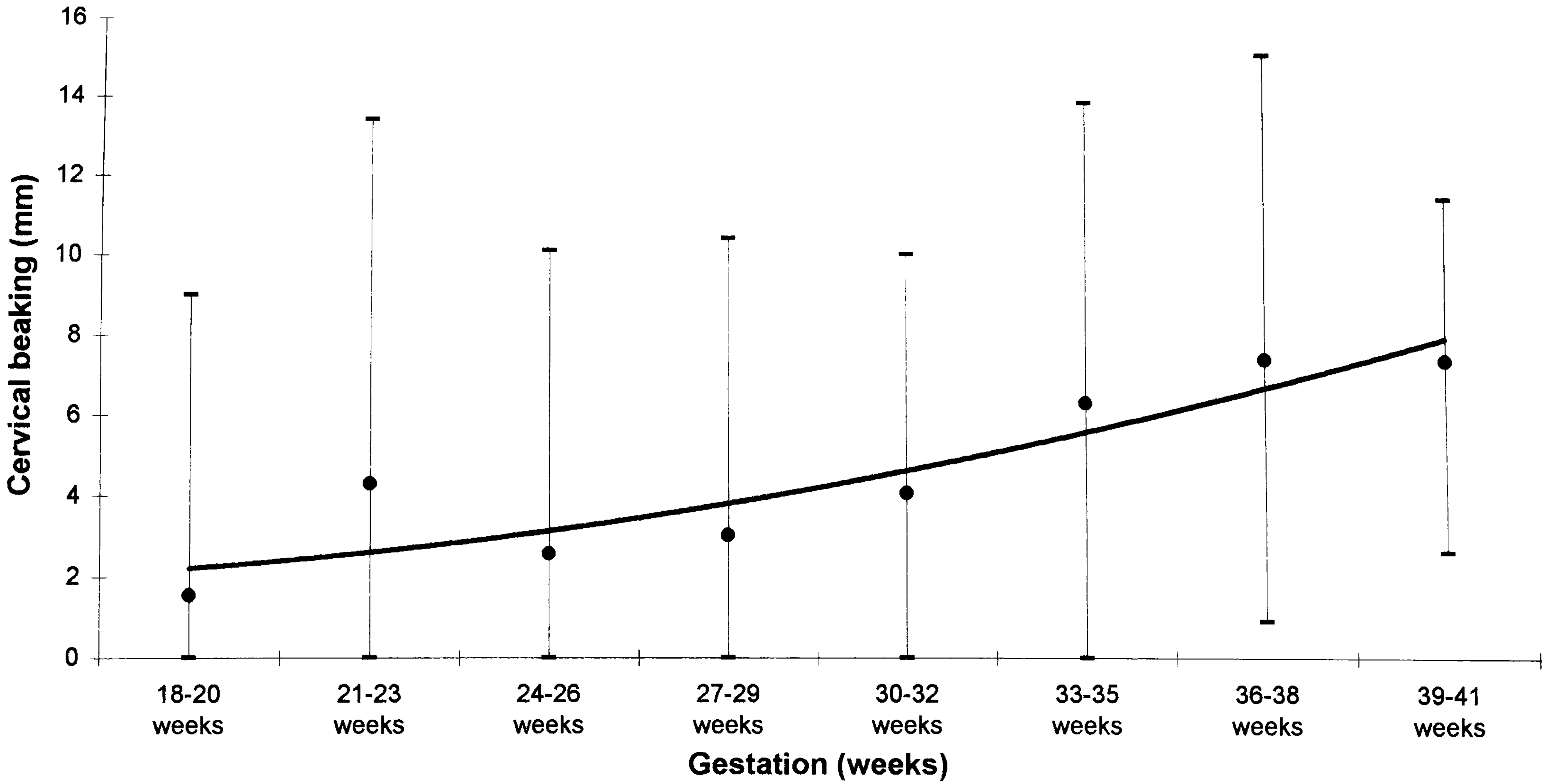


Figure 4.5 - Opening of the internal os; Low Risk population (mean +/- 5th-95th centiles)



Comparison of First and Subsequent Pregnancies

39% of those in the low risk group were primiparous, whilst 61% had had one or more previous term deliveries. As cervical length does vary with gestation, it is important to note that the gestation at first visit is comparable between the two groups (Table 4.2).

Table 4.2

Comparison between Primips and Multips: Gestation and Cervical lengths at first visit

	Mean gestation at first visit (sd)	**Mean cervical length at first visit (sd)**
Primips n = 20	20.35 weeks (2.41)	36.9 mm (6.88)
Multips n = 30	20.4 weeks (2.18)	38.4 mm (6.56)
Unpaired t-test	t = 0.08 NS	t = 0.32 NS

The difference in the mean cervical lengths of just over 1 mm is not a statistically significant difference, and is also within what would be expected as the intra-observer error in cervical measurements (4-5%: Zorzolli et al 1994). Equally, if gestation specific values are compared, primiparous and multiparous women do not differ significantly in cervical measurements at 18-20, 21-23 or 24-26 weeks gestation (Table 4.3). With no difference between them, combining the two groups to provide normal cervical values is appropriate.

Table 4.3

Comparison of Cervical Lengths in Primips and Multips in the 2nd Trimester

		Primips	Multips	Unpaired t- tests
		Mean (sd)	Mean (sd)	
Cervical Length	**18-20 weeks**	38.6 mm (7.76) n = 11	40.4 mm (7.14) n = 16	t = 0.63 p = 0.53
	21-23 weeks	35.3 mm (6.67) n = 12	35.5 mm (8.00) n = 27	t = 0.31 p = 0.76
	24-26 weeks	35.6 mm (6.25) n = 13	35.7 mm (8.67) n = 28	t = 0.04 p = 0.97

Previous terminations of pregnancy - does it influence cervical length?

A past history of terminations of pregnancy does carry an increased risk of a preterm delivery in the index pregnancy (Lumley 1993). In this low risk group, a total of 12 women had previously undergone one or more terminations of pregnancy. The comparison between the cervical lengths at 18-20 weeks and 21-23 weeks in these women and the rest of the low risk group are shown in Table 4.4. The difference in cervical length at 21-23 weeks was statistically significant ($p<0.038$). If however, the Bonferroni correction is used due to the use of several paired tests on the same data (previous TOPs, previous miscarriages and comparison of primps and multips; $k = 3$) then the statistical significance is lost ($p = 0.114$). This will be discussed further in Chapter 5. There was no difference in the cervical widths, whilst the large inter- and intra-subject variation in the cervical beak measurements precludes any meaningful comparison.

Table 4.4

Comparison of cervical lengths between those with and those without a past history of termination of pregnancy

	Cervical Length	
Previous TOPs	**18-20 weeks** **Mean (sd)** 35.0 mm (8.12) n = 4	**21-23 weeks** **Mean (sd)** 30.8 mm (4.56) n = 11
No history of TOPs	40.4 mm (7.04) n = 23	36.3 mm (7.96) n = 28
Unpaired t-test	t = 1.40 p = 0.18	t = 2.15 **p = 0.038**
Bonferroni correction k = 3	p = 0.54	p = 0.114

Past History of Miscarriage

A total of 11 women in the low risk group had a history of one or more first trimester miscarriage in a previous pregnancy. As distinct from those with a history of termination, no statistical significance could be demonstrated in the cervical length measurements at 18-20 or 21-23 weeks gestation between those with, and those without a history of a previous miscarriage (Table 4.5).

Table 4.5

Comparison of first cervical lengths of those with and those without a history of miscarriage

	Cervical length	
	18-20 weeks **Mean (sd)**	**21-23 weeks** **Mean (sd)**
Previous miscarriage	40.4 mm (8.98) n = 7	33.3 mm (9.70) n = 10
No past miscarriage	38.7 mm (6.38) n = 19	35.3 mm (6.77) n = 29
Unpaired t-test	t = 0.55 p = 0.59	t = 0.71 p = 0.48

Multiple Linear Regression Analysis

In this low risk cohort, both the gestation at delivery and the cervical length measurements have a Normal distribution, so allowing the use of multiple linear regression analysis to compare these measures to several other variables. Stepwise linear regression of the gestation at delivery against demographic and cervical measurements (Table 4.6) shows none are independently related to the gestation at delivery. A similar regression analysis against cervical length at 21-23 weeks does however show a weak correlation with the gestation at delivery, whilst the correlation at with cervical length at 24-26 weeks is stronger (Table 4.7).

Table 4.6

Factors included in Multiple Linear Regression Analysis against Gestation at Delivery

Smoking >10 per day	Cervical length at 18-20 weeks
Parity	Cervical length at 21-23 weeks
Number of terminations	Cervical length at 24-26 weeks
Number of miscarriages	Cervical beak at 18-20 weeks
Maximum change in cervical length 18-26 weeks	Cervical beak at 21-23 weeks
Maximum % change in cervical length 18-26 weeks	Cervical beak at 24-26 weeks

Table 4.7

Multiple Linear Regression Analysis against Cervical Length

Factors included in multiple linear regression analysis
Smoker >10 per day Parity Number of terminations Number of miscarriages Gestation at delivery

	Cervical Length at 21-23 weeks (mm)			
R^2 Value	**0.135**	**B Unstandardised coefficient**	**95% Confidence Intervals**	**p values**
Constant		-42.1	-104.8 to 20.6	
Gestation at delivery		1.962	0.36 to 3.56	**p = 0.021**

	Cervical Length at 24-26 weeks (mm)			
R^2 Value	**0.225**	**B Unstandardised coefficient**	**95% Confidence Intervals**	**p values**
Constant		-58.4	-144.14 to -10.05	
Gestation at delivery		2.879	1.169 to 4.589	**p = 0.002**

Discussion

These findings are similar to published reports of normal cervical values. Average cervical lengths reported have varied between 35 mm and 48 mm (Iams et al 1996, Kushnir et al 1990), with a commonly quoted "average" cervical length being 40 mm. This compares well with the measured average in our low risk group of 37.9 mm of first cervical length measurements taken in the second trimester and 35.5 mm of all measurements taken up to 32 weeks gestation.

Secondly, the pregnancy outcome data does demonstrate that this group was accurately identified as one at low risk of a preterm delivery. The preterm delivery rate was 2% whilst the mean gestation of delivery was 39.4 weeks. Meaningful comparisons between this data set and that produced from the high risk group to be discussed in Chapter 4 will hence be possible.

From the graphs shown, one aspect is clearly apparent; the cervix in pregnancy is not static, but progressively shortens and opens during pregnancy, not just in labour. In particular, there is significant and progressive cervical shortening from 30-32 weeks onwards (Figure 4.3). Clearly any discussion regarding cervical appearance of transvaginal ultrasonography needs to be gestation dependent. Cervical width is of less importance, with a lesser change with gestation and wider confidence intervals. Although there is a significant change in the opening of the internal os with gestation, the wide confidence intervals at each gestation and the wide variability of measurements within each subject over time make its use limited to cases of cervical incompetence or weakness, where there is far greater change at the internal os (Chapter 6). Although the results are important (in particular the demonstration of the change in cervical length over time) all three of these graphic presentations of the low risk cervical data need to be interpreted with caution. None can be used strictly as "normal" value charts such as those found for fetal measurements during pregnancy; to produce such a chart, for statistical accuracy each individual should be only measured once during the pregnancy, and a significantly greater number of subjects than was available to this study would be needed to produce accurate 5th and 95th centile ranges. Hence extrapolating from this data is inadvisable, although comparing single gestation measurements (or ranges of measurements) to those in the high risk group will be valid as this has been demonstrated to be a low risk group.

From the data presented here, neither parity nor a past history of miscarriage appear to have an impact on cervical length, but a past history of termination of pregnancy potentially does (Table 4.4). The Bonferroni correction takes the association at 18-20 weeks beyond statistical significance, but the association is significant within the larger cohort of the high risk group (Chapter 5), so a discussion of its relevance is worthwhile. This is potentially of importance, as it mirrors epidemiological evidence that a past history of a termination of pregnancy is associated with an increased risk of a preterm delivery in subsequent pregnancies (Lumley 1993). If there is a causative link, then one would expect it to be the cervical trauma caused by a termination. This then does bring forward the consideration that medical priming of the cervix with prostaglandins prior to any termination could be protective; investigation of cervical priming as a means of reducing the incidence of a future preterm delivery needs to be investigated. A short cervix has been associated with an increased risk of a premature delivery (Iams et al 1998, Heath et al 1998), and this association will be explored further in the next chapter, but this appears to be one of the most useful applications of transvaginal ultrasonography in pregnancy.

In conclusion, the main findings from this investigation of a low risk cohort were with regard to cervical length (rather than cervical width or beaking) and its associations. Normal cervical values are gestation dependent, particularly after 30-32 weeks, whilst measurements of primiparous and multiparous women were equivalent.

Subsequent Publications

Three large studies looking at cervical length on TVS in normal Obstetric populations have been published since 1995. Iams et al (1996) published a report of 2915 transvaginal scans at 24 weeks gestation in women recruited from several centres in America. The study population was designed to represent the general Obstetric population, and was not a specifically high risk group. Heath et al reported in 1998 an on going study of cervical length measurements at 23 weeks gestation of 2567 women. Again the study population was intended to reflect the general Obstetric population, as all women presenting to King's College Hospital were offered a transvaginal scan at 23 weeks; the reported acceptance rate was 80%. Taipale and Hiilesmaa reported a series of 3694 women scanned at between 18-22 weeks in what was clearly a low risk population with a preterm delivery rate of 2.4% (Taipale and Hiilesmaa 1998). Iams et al and Taipale and Hiilesmaa both reported their data in terms of the relative risk of a preterm delivery with regard to the centile of the cervical length. For Iams, the 50th centile was reported as 35 mm, with the 1st centile being 13 mm and carrying a relative risk of a preterm delivery compared to those above the 75th centile of 13.99. Taipale and Hiilesmaa reported a relative risk of 8 for a delivery before 35 weeks with a cervical length under 30 mm. Heath et al described their data in terms of percentages of the population with a specific cervical length, and the proportion of preterm deliveries within the group. The median cervical length was 38 mm, and 1.7% of the population had a cervical length of 15 mm or less. This 1.7% contained approximately 60% of those delivering before 32 weeks, and almost all those delivering before 26 weeks gestation.

A comparison of these large studies to the small sample in this study is difficult because of the size discrepancy. Equally, the entry criteria and recruitment were different; all recruited from the normal population, whilst our criteria separated the high and low risk. Even so, the reported median values of cervical lengths of 38 mm and 35 mm corresponds closely to our means for cervical length of 34.5 mm and 35.1 mm at 21-23 and 24-26 weeks gestation respectively (Figure 4.2).

The comparable studies to my research were done in the early 1990s (Zorzolli et al 1994, Murakawa et al 1993, Kushnir et al 1990), looking at low risk populations. The subsequent publications by Iams et al and Heath et al cover larger populations more representative of the total Obstetric cohort, and provide more information regarding the benefit of TVS looking at cervical length as a potential screening procedure.

Chapter 5

Transvaginal Ultrasound Assessment of the Cervix in the Second and Third Trimesters in Pregnancies at High Risk of Preterm Labour

Introduction

The identification of those women likely to have a pre-term delivery has consistently proved difficult. Risk factors have long been demonstrated for the risk of a pre-term delivery (Lumley 1993); factors such as past obstetric history, age, social class, smoking, race and weight all appear to have a bearing on the risk of a pre-term delivery. Several risk assessment scores have been proposed (Holbrook et al 1989, Creasy et al 1980), endeavoring to identify early in pregnancy those women with a significantly higher risk than average of a premature delivery. However, most methods of dividing women into 'high' and 'low' risk groups only identify less than 30% of those due to have a pre-term birth. For example Holbrook et al (1989) devised a risk scoring system to predict a preterm delivery which gave a sensitivity of 41% and positive predictive value of 25%.

Recently several other approaches have been followed in an effort to improve the accuracy of predictions and also to target treatment at those most in need. Detailed investigation of vaginal flora has implicated several organisms (or groups of organisms) in producing an increased risk of prematurity; bacterial vaginosis (Hay et al 1994), group B streptococcus (Alger et al 1988) and mycoplasmas and ureaplasmas have all been identified more frequently in women who deliver preterm compared to those who deliver at term. However, the increased risk of a preterm delivery due to carriage of bacterial vaginosis, which appears to be the most significant colonisation, is a relative risk of 1.5-2, which is no better than risk assessment profiles.

The identification of fetal fibronectin in vaginal secretions has provided a potential improvement in our identification of high risk pregnancies. Recent publications have demonstrated that a high vaginal swab positive for fetal fibronectin at 24 to 26 weeks carries a relative risk of a delivery before 32 weeks of 59 (Goldenberg et al 1996); this compares to the bacterial vaginosis relative risk of 2 and a relative risk of a past pre-term delivery of 10. The suggestion has been proposed that the presence of fetal fibronectin is indicative of some disruption to the fetal membranes, perhaps due to infection (vaginal or endometrial), but the causation is not yet defined. A positive fetal fibronectin test has an excellent sensitivity and specificity for a delivery before 28 weeks gestation of 63% and 98% respectively, but a positive predictive value of only 13% (Goldenberg et al 1996). The test is expensive and at present gives us no guide to treatment. Further research and investigation is required.

The third approach to identify those at high risk of pre-term labour has been the use of transvaginal ultrasonography. Several studies have demonstrated a definite correlation between cervical length as seen on transvaginal ultrasonography with past obstetric performance (Iams et al 1995) and also the risk of a pre-term delivery in the present pregnancy (Anderson et al 1994, Iams et al 1994, Iams et al 1996, Iams et al 1998). Further investigation of the cervix seemed worthwhile on two grounds. Firstly, much of the work so far published has come from America, where the use of antenatal interventions (cervical cerclage, antibiotics and tocolytics) is commonly higher than in

Britain. Secondly, few reports have compared low and high risk populations from the same region within the same study, making identification of risk factors potentially difficult. This tends to make interpretation of the ultrasonographic findings difficult and provides the basis for a largely observational study of the cervix during the pregnancies of women felt to be at high risk of a preterm delivery.

Study Design

As with the investigation of the low risk group described in Chapter 3, this study of the high risk population was designed to be observational, but with intervention allowed on the basis of specific cervical appearances on TVS; a cut off of 10 mm for the cervical length was used, partly as this would represent a cervix about a quarter the normal length of 35-40 mm and partly as this was an educated guess as what would constitute an abnormally short cervix. Following the start of the study, the same cut off for intervention of 10 mm was used by Guzman et al (1997) and was shown by Iams et al (1996) to be below the 99th centile for cervical length.

Method

The methods for recruitment and scanning have been described in Chapter 2. Not uncommonly, either due to maternal request or due to changes in the cervical appearance over time, women in the high risk group were scanned more frequently than every 3 weeks. In view of the increased risk of a pre-term delivery in these women, the option of prophylactic steroids (to promote fetal lung maturity in case of a pre-term delivery) was discussed with this group, and was taken up by approximately

30%, either due to maternal request, consultant advice or as a response to the cervical appearance on TVS.

This study was designed to be observational, but specific end points were decided at the outset: amniotic membranes visible on speculum examination, or a cervical length (internal to external os as measured on TVS) less than 10 mm. At this stage the consultant in charge was informed of the ultrasound findings and a decision whether to intervene (usually in the form of a cervical cerclage) was taken .

The aim was to follow all women up to at least 34 weeks; scans beyond this gestation were undertaken on an individual basis should the pregnant woman involved wish to continue.

Setting

All scans were performed in the Cotswold Centre for Women's Health, Southmead Hospital on an Ultramark 4-Plus ultrasound scanner, using a 5.0MHz vaginal probe, and a 3.5MHz linear sector transabdominal probe.

Study Duration

December 1995 - September 1997

Results

Demographics

A total of 106 women were recruited into the high risk group. The age range of recruits was 15 to 42 years (mean = 29.6 years, median = 30 years, sd = 4.9). The reason for recruitment in the majority of cases was due to a previous pre-term delivery; past obstetric histories are shown in Table 5.1.

Table 5.1

Past Obstetric History of Women in the High Risk Group (n = 106)

	Total number in the high risk group
First trimester losses	50
Second trimester losses	27
Terminations of pregnancy	37
Terminations x2	5
Terminations x3	3
Pre-term deliveries	109
Pre-term deliveries before 32/40	39
Term deliveries	75
Average gestation at delivery of all pregnancies beyond the first trimester	32.9 weeks

34 (32%) were smokers of more than 10 cigarettes per day, with 72 (68%) non-smokers or occasional smokers (less than 10 cigarettes per day). Only one primip was recruited; she was aged 15 years at conception, smoked 15-20 cigarettes per day

and was recruited at 24 weeks gestation following admission with abdominal pain; she delivered at 27 weeks.

Recruitment was largely via the Antenatal Clinic, although a few were seen and recruited on admission to hospital, and two, having had friends involved in the study, rang to ask to be included. The median gestation for recruitment was 18 weeks (range = 10-29 weeks). Over 650 separate transvaginal and transabdominal scans were performed, with an average of 6.1 visits per individual (range = 1-15).

Pregnancy Outcome

Table 5.2

Mode of Delivery

Type of Delivery	Number in High Risk group
Normal vaginal delivery	88 (83%)
Elective Caesarean	7 (6.5%)
Emergency Caesarean	7 (6.5%)
Ventouse delivery	2 (2%)
Forceps delivery	2 (2%)

The modes of delivery are shown in Table 5.3. Two women were lost to follow up during the third trimester but the pregnancy outcomes are known so the results are included. A total of 17 women within the high risk group had cervical sutures inserted; six were sutured electively in the second trimester on the basis of a consultant decision due to the past obstetric history, whilst the remaining eleven were sutured between 15 and 25 weeks as a result of the cervical appearance on transvaginal ultrasound. As well as being considered part of the high risk group for the purposes of these results, the ultrasound appearances and outcome in these nine women will also be examined separately in the next chapter.

Second Trimester Losses

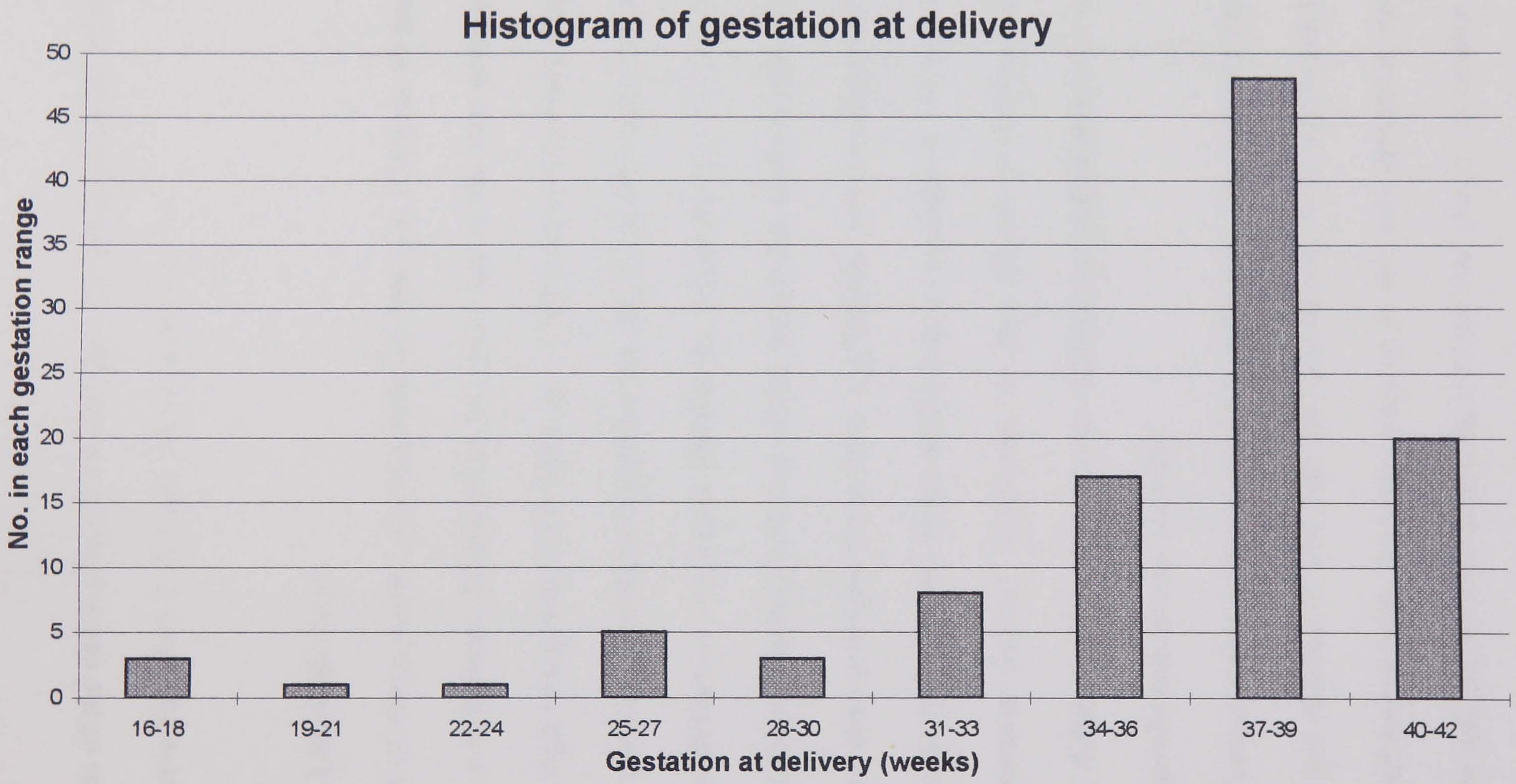
Five pregnancies ended in the second trimester; one terminated at 21 weeks for a 13/21 chromosomal translocation found after an amniocentesis, one miscarried at 16 week after bleeding , one missed miscarriage was found at 18 weeks, one ended at 23 weeks when an abruption caused fetal demise prior to delivery, and one miscarried at 18 weeks due to an E.Coli septicaemia following two cervical cerclage procedures for cervical incompetence.

Gestation at Delivery

The median gestation at delivery was 38 weeks (mean = 35.9 weeks, range = 16-42 weeks, sd = 5.2) with five second trimester losses and 33 preterm deliveries (31% of the high risk group). Twelve deliveries (11% of the high risk group) occurred before 32 weeks (Figure 5.1). The comparable population figures commonly quoted are 5-9% of babies born prematurely, and 1.5% born before 32 weeks gestation. In comparison the low risk group from Southmead Hospital (Chapter 4) had a 2% preterm delivery rate, with none before 32 weeks.

In view of the wide variation in gestation at delivery, birthweights also varied significantly. The median birthweight was 3095g (range 650-4580g).

Figure 5.1



Histogram of gestation at delivery
No. in each gestation range
0
5
10
15
20
25
30
35
40
45
50
16-18
19-21
22-24
25-27
28-30
31-33
34-36
37-39
40-42
Gestation at delivery (weeks)

Cervical Data

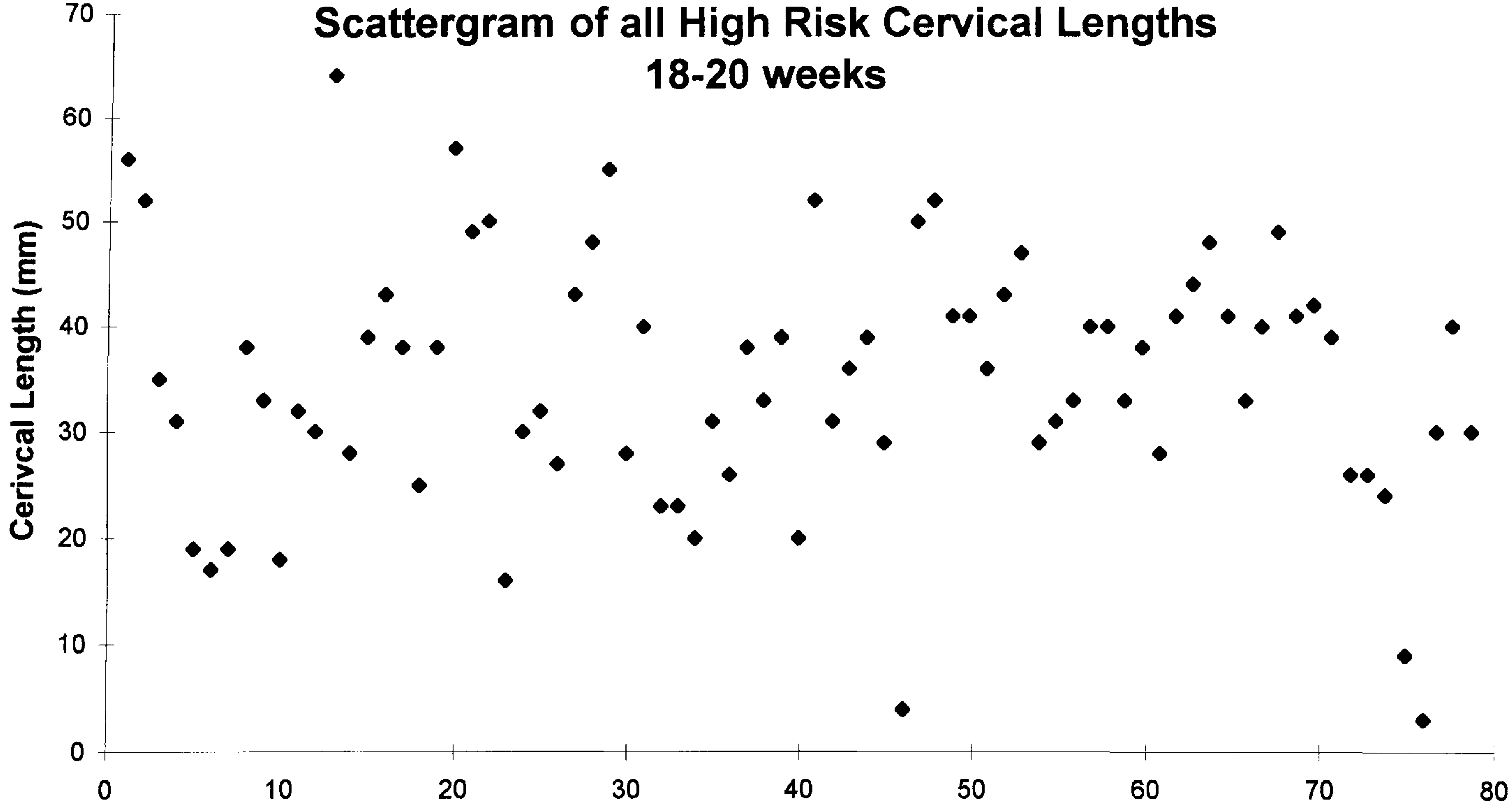
Scattergrams of the cervical lengths in the high risk group at 18-20, 21-23 and 24-26 weeks are shown in Figures 5.2, 5.3 and 5.4 respectively.

Comparison with Low Risk data

Comparison of demographic data between the low risk (Chapter 4) and the high risk groups shows a significant difference in the mean age in the two groups (low risk group; 28.1 years: high risk group; 29.6 years, p = 0.035, unpaired t-test). Only 16% of the low risk group smoked 10 or more cigarettes per day, compared with 33% in the high risk group, and this difference was again statistically significant (p = 0.023, unpaired t-test); a likely result, given smoking was one of the criteria for division into high and low risk categories. Also unsurprisingly, there were significantly more multiparous women in the high risk cohort, as the main risk factor which lead to inclusion in the high risk group was a previous preterm delivery. However, as was shown in Chapter 4, cervical dimensions do not differ significantly between multiparous and primiparous women, so comparisons between the two groups are valid.

Graphical demonstration of the cervical changes over time (as was shown in the low risk group) is not relevant in this high risk population. As a significant proportion (over 30%) delivered before term, the data collected at the later gestations more closely correlates to the low risk population rather than the high risk group - in essence a form of self selection. Comparison between the low and high risk groups in the second and early third trimesters is however still valid.

Figure 5.2
Scattergram of all High Risk Cervical Lengths
18-20 weeks



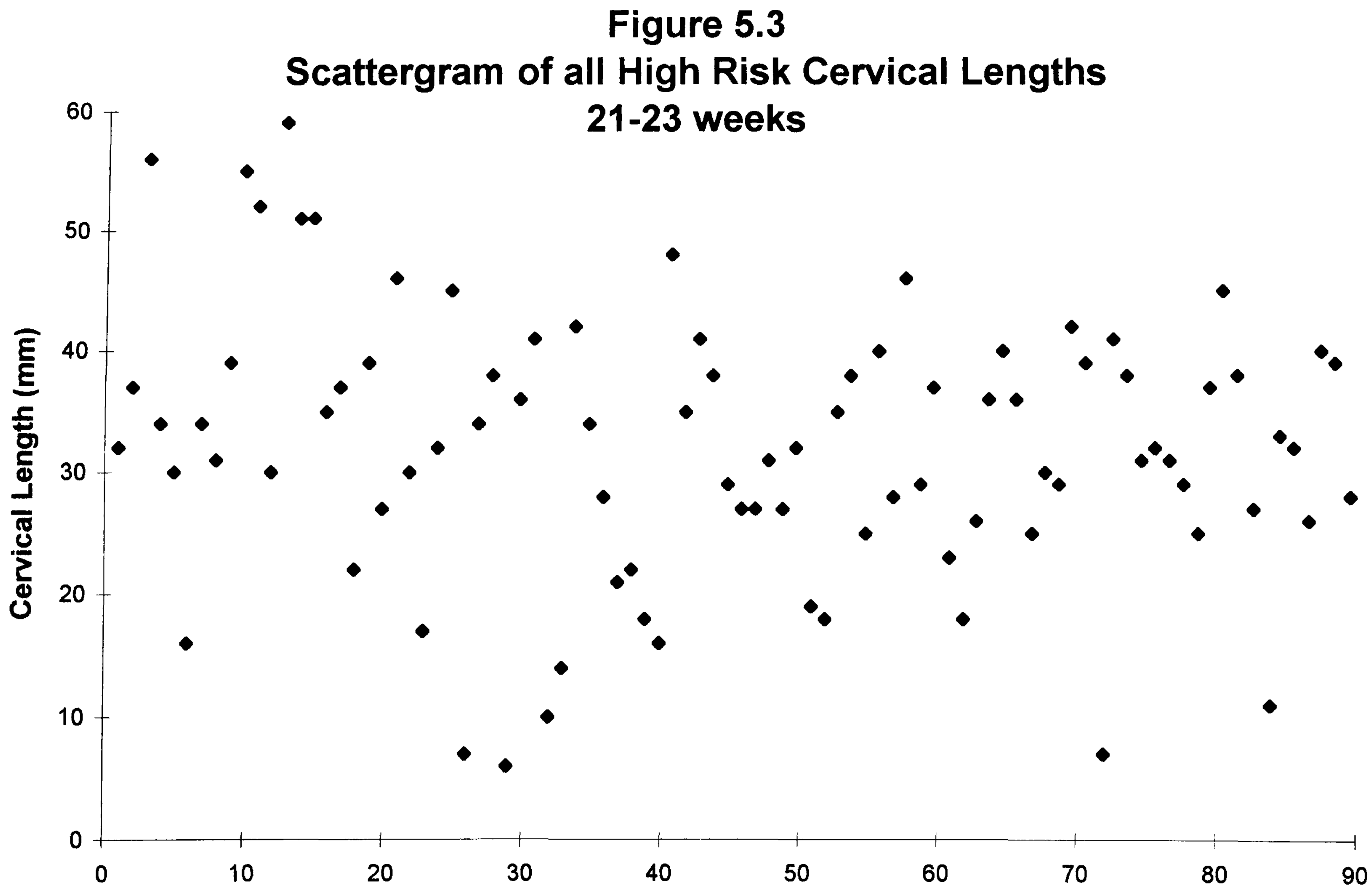


Figure 5.3
Scattergram of all High Risk Cervical Lengths
21-23 weeks
Cervical Length (mm)
0
10
20
30
40
50
60
0
10
20
30
40
50
60
70
80
90

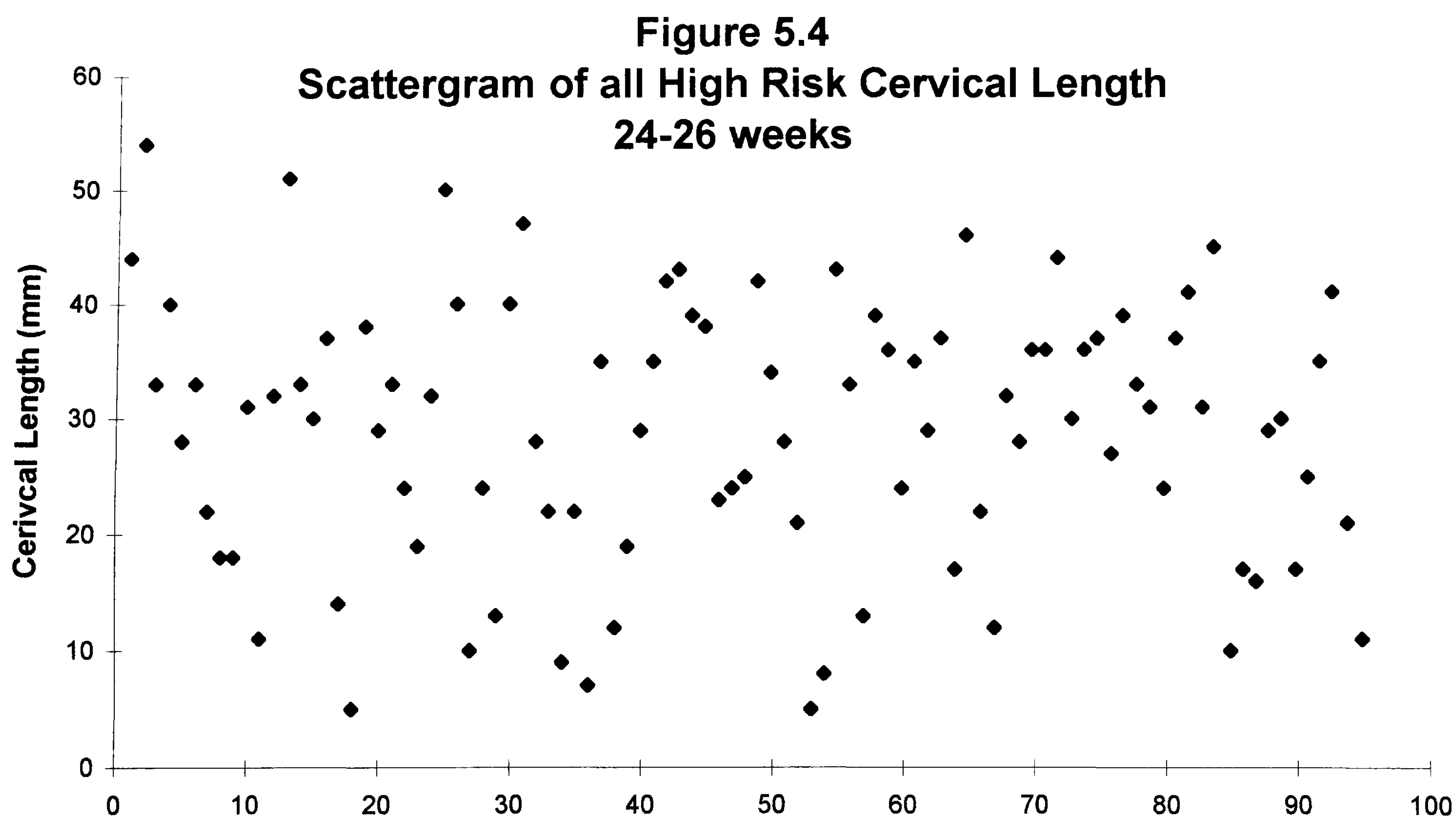


Figure 5.4
Scattergram of all High Risk Cervical Length
24-26 weeks
Cerivcal Length (mm)
0
10
20
30
40
50
60
0
10
20
30
40
50
60
70
80
90
100

There is a significant difference between the low risk and high risk cohorts with regard to the gestation at recruitment (low risk mean; 20.4 weeks, high risk; 18.2 weeks). Many of the high risk group were seen early in the second trimester due to either their own or their consultant's concern with regard to a further preterm delivery. Comparison between the two groups will hence be advisable on a gestation specific basis, not based on first visit cervical measures.

Cervical Comparisons at Different Gestations

Cervical Length

Comparing cervical lengths at specific gestations, no statistical difference in cervical length is apparent at 18-20 weeks either between those in the high risk group and those in the low risk, or between those in the high risk group who had a preterm delivery compared to those who had a term delivery. However, at 21-23 weeks the differences are statistically significant between those who delivered at term compared to preterm within the high risk group, whilst a significant difference between the high and low risk groups is apparent at 24-26 weeks (Table 5.3).

Cervical Width and Cervical Beaking

A comparison of cervical widths shows no difference between the high and low risk groups (preterm or term deliveries), whilst with regard to the opening of the internal os (cervical "beaking"), statistically significant differences were apparent at 24-26 weeks between the high and low risk groups, and also between the preterm and term deliveries in the high risk cohort (Table 5.4).

Table 5.3

Comparison of cervical lengths at different gestations

	Mean cervical length (sd)		
	18-20 weeks	**21-23 weeks**	**24-26 weeks**
Low risk cohort	39.6 mm (7.18) n = 28	34.7 mm (7.52) n = 39	35.6 mm (7.98) n = 40
High risk cohort	36.1 mm (11.72) n = 72	32.8 mm (10.84) n = 83	29.9 mm (11.89) n = 91
Unpaired t-tests	t = 1.49 p = 0.14	t = 0.97 p = 0.34	t = 2.77 **p = 0.007**
High risk - term delivery	36.6 mm (11.72) n = 47	34.6 mm (9.73) n = 58	31.5 mm (11.03) n = 61
High risk - preterm delivery	35.2 mm (11.91) n = 25	28.7 mm (12.28) n = 25	26.6 mm (13.03) n = 30
Unpaired t-tests	t = 0.47 p = 0.63	t = 2.33 **p = 0.02**	t = 1.88 p = 0.08

Table 5.4

Comparison of Cervical beaking at different gestations

	Cervical beak Mean (sd) 21-23 weeks	24-26 weeks
Low risk cohort	3.7 mm (4.64) n = 31	2.7 mm (3.79) n = 38
High risk cohort	5.2 mm (6.12) n = 58	5.8 mm (6.37) n = 59
Unpaired t-tests	t = 1.23 p = 0.22	t = 2.69 **p = 0.008**
High risk - term delivery	4.9 mm (6.22) n = 41	4.5 mm (5.69) n = 41
High risk - preterm delivery	5.9 mm (6.02) n = 17	8.8 mm (6.94) n = 18
Unpaired t-tests	t = 0.57 p = 0.57	t = 2.54 **p = 0.01**

Cervical Appearance and a Past History of Termination of Pregnancy

In the low risk cohort, a potential association between previous terminations of pregnancy and a short cervix was found. This finding was confirmed in the high risk cohort. At both 18-20 and 21-23 weeks, a past history of termination of pregnancy was associated with a significantly shorter cervix (Table 5.5). There was no association with either the cervical width or the cervical beak. Unlike the low risk cohort, there was a significant association at 21-23 weeks between a history of previous miscarriages and the cervical length (p = 0.01). Even with the Bonferroni correction for multiple paired tests (k = 3; TOPs, miscarriage and high and low risk cohorts) there is still a significant association between a past history of TOPs and cervical length at 18-20 weeks (p = 0.009), and a past history of miscarriage (p = 0.03).

Table 5.5

Comparison of Cervical Length in those with and without a past history of Termination of Pregnancy

	Cervical Length Mean (sd)		
	18-20 weeks	**21-23 weeks**	**24-26 weeks**
Previous TOPs	29.0 mm (12.52) n = 19	28.5 mm (11.23) n = 21	25.6 mm (9.52) n = 16
No TOPs	38.3 mm (10.78) n = 54	34.3 mm (10.47) n = 62	31.1 mm (11.74) n = 63
Unpaired t-tests	t = 3.11 **p = 0.003**	t = 2.14 **p = 0.036**	t = 1.72 p = 0.09
Bonferroni correction k = 3	**p = 0.009**	p = 0.108	p = 0.27

High Risk Group and Cervical Cerclage

A subset of 17 women within the high risk group received a cervical cerclage; six as an elective procedure, and 11 as a consequence of the ultrasound appearance or the clinical picture. In this subgroup of the high risk population, there had been a total of 22 previous late second trimester losses or preterm deliveries and nine previous term deliveries (Table 5.6).

Table 5.6

Past Obstetric History of Patients with a Cervical Cerclage

	Elective Cerclage (n = 6)	Emergency Cerclage (n = 11)	All Cerclage Patients (n = 17)
Median gestation of previous preterm deliveries	23.5 weeks (n = 9)	22 weeks (n = 13)	23 weeks (n = 22)
Median gestation of previous term deliveries	39 weeks (n = 6)	40 weeks (n = 3)	40 weeks (n = 9)
Median gestation of all previous deliveries	26 weeks (n = 15)	22.5 weeks (n = 16)	26 weeks (n = 31)
Number of patients with three previous TOPs	0	2	2

When comparing those sutured electively and those sutured as an emergency, there was no significant difference in the gestation of previous deliveries. Those sutured electively had several more term deliveries, but five out of six had had previous cervical cerclage which could account for the difference in pregnancy outcome. The one difference of note was that the emergency cerclage group had the only two women to have had three previous terminations of pregnancy each.

The gestation of cerclage was unsurprisingly different; a median of 13 weeks (range 12-13) in the elective cerclage group, whilst the emergency group median gestation for cerclage was 21 weeks (range 15-26). On transvaginal ultrasound, only two of the six electively sutured had evidence of cervical shortening or opening of the internal os either before or after cerclage, whilst 9 out of 11 of the emergency group demonstrated cervical change (shortening over time or opening of the internal os) before the suture was inserted. Of the two who did not, one was sutured on consultant recommendation because of a short cervix on TVS (but >10 mm) and a history of a previous 28 week delivery (and delivered again at 28 weeks after preterm prelabour ruptured membranes), and one was sutured as an emergency having been admitted with a backache, vaginal discharge and membranes bulging through a partly dilated cervix at 26 weeks; she delivered one week later.

Gestation at delivery

In all 17 women sutured, there were nine preterm deliveries, with six occurring before 32 weeks gestation. The median gestation of delivery was 36 weeks. To compare effectively between the elective and emergency cerclage based on ultrasound views the two women who were sutured as an emergency on clinical, not ultrasound grounds will not be included. The gestation at delivery of the remaining 15 is shown in Table 5.7 and

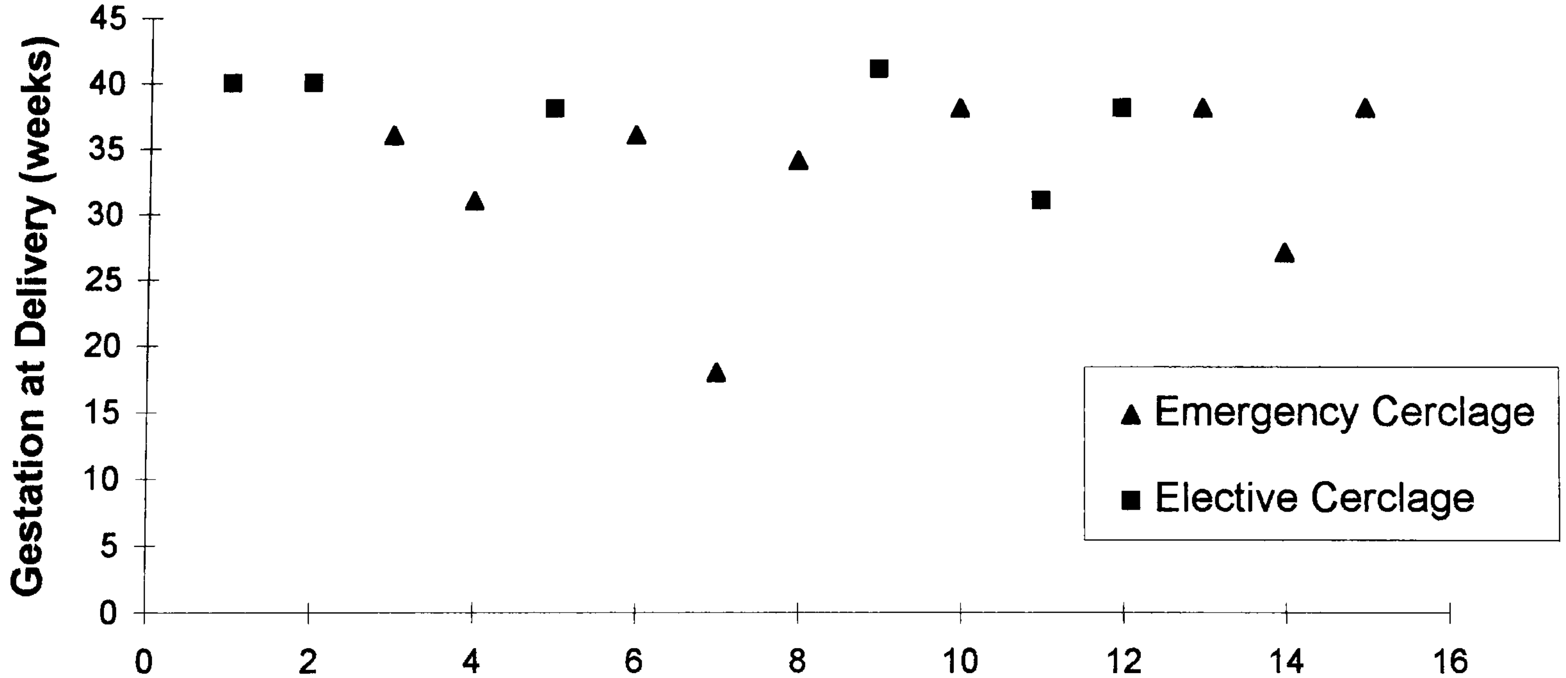
Figure 5.5. The gestation at delivery was normally distributed so an unpaired t-test was appropriate.

Table 5.7

Gestation at Delivery; Elective vs. Emergency Cerclage

	Mean Gestation at Delivery (sd)
Elective Cerclage (n = 6)	38.0 weeks (3.6)
Emergency Cerclage (n = 9)	32.9 weeks (6.7)
Unpaired t-test	t = 1.70 p = 0.11 CI = -1.4 to 11.6

Figure 5.5
Gestation at Delivery
Emergency and Elective Cerclage



From the figures presented there is no statistical difference in the gestation at delivery between those sutured electively and those sutured as a result of the ultrasound appearance, although the means appear widely separated (32.9 and 38 weeks). There are three potential ways of interpreting these results. Firstly, as the numbers are indeed too small it is possible that with larger numbers a statistical difference would become apparent, demonstrating that elective cerclage has a distinct advantage over cerclage following the onset of cervical change. Calculation of the power of the study (Altman 1982) suggests that, if the difference between the elective and emergency cerclage groups in terms of gestation at delivery remained at 5.1 weeks (Table 5.7), for an 80% power of the study and a p value of 0.05, a sample size of over 45 patients (more than 22 patients per arm; three times the size of the present study) would be required to demonstrate a statistical difference. The second interpretation would be that a difference between the two groups would become apparent with larger numbers, but that this is due to the "normality" of the electively sutured group; only two out of six had cervical change before cerclage. This I feel is not appropriate, as the earlier suturing in the elective group occurred at a gestation at which none of the emergency group had cervical change on scan; this is unlikely to be the reason for any difference. The third possibility is that there is no difference in risk of a preterm delivery between an early elective suture and one delayed until after cervical change is seen on ultrasound. This is an important consideration; cervical cerclage is not without maternal and fetal risks, and it was apparent from the MRC/RCOG trial into cervical cerclage (1993) that the clinical diagnosis of cervical cerclage is not accurate.

Hence if it were safe to wait until cervical change were noted on scan before attempting a cervical cerclage, potentially it would be possible to avoid the unnecessary sutures and the risks that a suture can entail. The numbers are too small to answer this question, but question raised from this group as to future treatment is an important one and needs investigation. A review of the literature published since the onset of this research with regard to elective and emergency cerclage will be presented at the end of this chapter.

Multiple Linear Regression Analysis

Gestation at Delivery

Numerous factors are known to influence the likelihood of a preterm delivery (Lumley 1993), and investigating other factors known to be associated with preterm deliveries as well as the cervical appearance is advisable. Risk factors for a preterm delivery include the past obstetric history (preterm deliveries, second trimester miscarriages, previous terminations of pregnancy and previous miscarriages), smoking, age and the presence or absence of vaginal infections such as BV and GBS (Holbrook et al 1989, Creasy et al 1980, Lumley 1993, Hay et al 1994). Multiple linear regression analysis was performed to investigate whether the significance of all these factors (and cervical appearance) could be separated out in our population. Gestation at delivery did not have a Normal distribution, so the data was transformed; firstly by converting it to number of weeks before 42 weeks gestation that delivery occurred (e.g. delivery at 32 weeks gestation being regarded as +10), with a $\log_e$ transformation of this data to produce a Normal distribution appropriate for use as the outcome measure in linear regression analysis. The variables used in the linear regression analysis are shown in Table 5.8.

Comparing this transformed gestation at delivery data, three factors were found to be independent variables; cervical length at 21-23 weeks, the number of previous preterm deliveries, and the maximum change in the cervical length from 18-26 weeks.

Table 5.8

Multiple Linear Regression Analysis against Gestation at Delivery

Variables used in Multiple Linear Regression Analysis		
Parity	Cervical length at 18-20 weeks	Cervical beak at 18-20 weeks
Smoking >10 per day	Cervical length at 21-23 weeks	Cervical beak at 21-23 weeks
Number of terminations	Cervical length at 24-26 weeks	Cervical beak at 24-26 weeks
Number of miscarriages	Previous deliveries 16-24 weeks	Cervical length change 18-23 weeks
Number of previous preterm deliveries	Previous deliveries 24-32 weeks	Cervical length change 21-26 weeks
Age at conception	Previous deliveries 33-35 weeks	Cervical length change 18-26 weeks
	Maximum cervical length change 18-26 weeks	Maximum % cervical length change 18-26 weeks

Multiple Linear Regression Analysis: Gestation at Delivery

	Log_e of time before 42 weeks gestation for delivery		
R^2 Value	**0.532**		
	B Unstandardised Coefficient	**95% Confidence Intervals**	**p values**
Constant	1.263	0.64 to 1.89	
Cervical length 21-23 weeks	-0.016	-0.13 to 0.10	**p = 0.014**
Number of preterm deliveries	0.325	0.14 to 0.51	**p = 0.002**
Maximum cervical length change 18-26 weeks	0.029	0.009 to 0.049	**p = 0.007**

Cervical Length

Cervical length, unlike the gestation at delivery, did have a Normal distribution, so linear regression against cervical length was possible. The variables used are shown in Table 5.9.

Table 5.9

Multiple Linear Regression against Cervical Length

Variables used in multiple linear regression analysis	
Parity	
Smoker >10 per day	Previous delivery at 16-24 weeks
Number of terminations	Previous delivery at 24-32 weeks
Number of miscarriages	Previous delivery at 33-35 weeks
Number of previous preterm deliveries	Gestation at delivery

The greatest correlation indicated by the R^2 value occurred at 21-23 weeks gestation ($R^2 = 0.257$, compared to 0.175 at 18-20 weeks and 0.157 at 24-26 weeks) - Table 5.10. At this gestation the independent variables were a previous delivery at 16-24 weeks, the number of previous preterm deliveries, parity and the number of previous terminations of pregnancy.

Table 5.10

Linear Regression Analysis Results for Cervical Length at 21-23 weeks gestation

	Cervical Length at 21-23 weeks (mm)		
R^2 Value	**0.257**		
	B Unstandardised Coefficient	**95% Confidence Intervals**	**p values**
Constant	45.67	37.76 to 53.58	
Previous delivery 16-24 weeks	-5.02	-10.10 to 0.06	p = 0.056
Number of previous preterm deliveries	-7.42	-11.58 to -3.26	**p = 0.001**
Parity	2.28	0.43 to 4.12	**p = 0.018**
Number of terminations	-3.23	-2.07 to -4.39	**p = 0.046**

Predictive Value

One important consideration with any investigation into pregnancies at high risk of a preterm delivery is whether the method under investigation is more useful than the present risk assessment used. The classification of women into a "high" and "low" risk groups produced a sensitivity (how good the test is at identifying those how will deliver preterm) of 0.97, a specificity (how good the test is at excluding those who will deliver at term) of 0.42, and a positive predictive value of the screening test (the chance of delivering preterm if the test is positive) of 0.36 (Table 5.11).

Table 5.11

High versus Low risk categorisation

	Preterm delivery	Term delivery	Totals
High risk	38	68	106
Low risk	1	50	51
Totals	39	118	

Sensitivity	**0.97**
Specificity	**0.42**
PPV	**0.36**

Relative Risk **17.85**
(CI 3.44 - 92.11)

From the linear regression analysis, cervical length at 21-23 weeks gestation and the maximum change in cervical length over 18-26 weeks appear the most significant independent cervical variables. Using a cervical length of 25 mm or less at 21-23 weeks as a cut off from the study data, the sensitivity of the test is 0.45, specificity 0.85 and positive predictive value 0.47 (Table 5.12). If the division between "high" and "low" risk was determined by a cervical length shortening by 15 mm or more, the sensitivity is 0.4, the specificity 0.94 and positive predictive value 0.62. (Table 5.13).

Table 5.12

Cervical Length at 21-23 weeks

	Preterm delivery	**Term delivery**	**Totals**
Cervical length </= 25 mm	16	18	34
Cervical length > 25 mm	19	99	118
Totals	35	117	

Sensitivity	**0.46**
Specificity	**0.85**
PPV	**0.47**

Relative Risk **2.92**
(CI 1.8-4.6)

Table 5.13

Maximum Cervical Length Shortening

	Preterm delivery	Term delivery	Totals
Maximum cervical length shortening >/= 15 mm	10	6	16
Maximum cervical length shortening < 15 mm	15	101	116
Totals	25	107	

Sensitivity	**0.4**
Specificity	**0.94**
PPV	**0.63**

Relative Risk **4.83**
(CI 2.91 - 8.03)

Discussion

Several conclusions can be drawn from the data presented in this Chapter. As with the low risk cohort (Chapter 4) the screening process to determine "high" and "low" risk of a preterm delivery does seem appropriate; 31% in the high risk cohort delivered prematurely, with 36% delivering either preterm or late in the second trimester.

Comparison with the Low Risk Cohort

In comparison with the low risk cohort, two demographic differences stand out. The high risk group were statistically older and also contained more women who smoked 10 or more cigarettes per day. However as multiparous women tend to be older, and a previous preterm delivery and a history of smoking were criteria for entry into the high risk group, neither of these findings are surprising. Interestingly though, despite being a risk factor for a preterm delivery, smoking was not a significant independent variable in the linear regression analysis with regard to the gestation at delivery.

Cervical comparison with the low risk cohort shows no difference in the cervical width, but significant differences in the cervical length and opening of the internal os at 21-23 weeks but not before this gestation. Although statistically significant, the difference in the cervical beaking will be difficult to take forward in any practical sense; the variation within and between individuals is enormous (ten to 12-fold differences over 1-4 weeks), making interpretation and prediction from future results limited. Cervical length on the other hand is less variable both between and within individuals and is likely to be of more relevance in future assessment of risk of a preterm delivery. There was no significant difference between the high and low risk cohorts at the earlier gestations (18-20 weeks), but a statistically significant difference in cervical length was apparent from 21 weeks onwards. This ties in well with the significance in predicting a preterm delivery of a short cervix measured at 23 weeks gestation reported by Heath et al (1998). From what we have found, measurement of the cervical length prior to 21 weeks may not be able to discriminate effectively between those women destined to deliver at term and those in whom a preterm delivery is a possibility.

Termination of Pregnancy

Comparison with the low risk cohort indicated that the cervical measurement at 21-23 weeks provided the most differential between the two groups. The same gestation is of relevance in providing a distinction between those with and those without a past history of termination. The difference seen, but not statistically significant, within the low risk group was significant in the high risk group; those with a past history of termination having a significantly shorter cervix at 18-20 weeks, and this association was also demonstrated in the linear regression analysis, in which a past history of termination was shown to be an independent variable with regard to cervical length. Although in this study the past terminations were not associated with an increased preterm delivery rate, this has been noted in previous studies (Lumley 1993, Holbrook et al 1989), as has the association between a short cervix and preterm delivery (Iams et al 1996, Heath et al 1998). It is tempting to extrapolate that potentially the greater the surgical manipulation of the cervix (either in terms of several first trimester terminations or one later second trimester termination) the shorter the subsequent cervix and hence the increased risk of a preterm delivery. With regard to this issue, no investigation in this study was made into past histories of a dilatation and curettage, either as a diagnostic procedure or in relation to a miscarriage, but this would be worth investigating in a future study since there appears to be an association between terminations, previous miscarriages and subsequent cervical length. One potential area of future investigation would be a prospective trial looking at cervical measurement before a termination of pregnancy and then in a subsequent pregnancy.

Prediction of Preterm Delivery

The prediction of preterm labour is at present both imprecise and difficult. On the basis of the women's past obstetric history in this trial, 36% of those designated "high risk" delivered prematurely. If the same women were divided on the basis of their cervical appearance at 21-23 weeks, 47% in the "high risk" categories delivered prematurely. If the categorisation was done on the basis of the maximum cervical change occurring between 18-26 weeks, 63% in the "high risk" category delivered before 37 weeks gestation (Tables 5.11 - 5.13, positive predictive values). However, both cervical measures do have only modest sensitivities and relative risks (Tables 5.12, 5.13) which means predictions of future pregnancies from these results will be of limited value. What is of greater relevance is that, from the linear regression analysis, two cervical measures (cervical length at 21-23 weeks and the maximum change in cervical length) were independent variables with regard to gestation at delivery, with the only other independent variable being a past history of preterm delivery. Past scoring systems have concentrated on demographic and obstetric factors such as previous preterm deliveries (Holbrook et al 1989, Creasy et al 1980) but up to the time of the start of this research, just four paper had identified the association between a short cervix and the increased risk of a preterm delivery (Andersen et al 1990, Murakawa et al 1993, Iams et al 1994 and 1995). In these cases, individual measurements were investigated, whilst the new factor coming from this research has been the importance of the cervical change over time as being a significant factor in determining the risk of a preterm delivery. Future research into cervical change as well as individual measures at a single point in time will be important.

Subsequent Publications

There has been a mushrooming of publications on transvaginal ultrasonography and the cervix in pregnancy since the inception of our research in 1995. Four publications between 1996 and 1999 have dealt with longitudinal approach to the cervix during pregnancy (Table 5.14), whilst a further 17 investigated the role of TVS with regard to past Obstetric history and the risk of a preterm delivery (Table 5.15).

Table 5.14

Publications of longitudinal data on cervical length 1995-1999

Author	Journal	Year	Number of patients	Gestation of scans	Reason for study
Iams et al	N Eng J Med	1996	2915	24 and 28 weeks	Assessment of the risk of preterm delivery based on cervical length
Cook et al	Br J Obstet Gynaecol	1996	41	18-30 weeks	Longitudinal study of the cervix
Brieger et al	Acta Obstet Gynecol Scand	1997	55	30-36 weeks	Assessment of cervical change during the third trimester
Guzman et al	Obstet Gynecol	1998	61	15-24 weeks	Cervical change in those at risk of cervical incompetence

Table 5.15

Publications on TVS and the risk of Preterm delivery

1996-1999

Author	Journal	Year	Number of patients	Gestation of scans	Reason for study
Timor-Tritsch et al	Am J Obstet Gynecol	1996	70	Threatened prem labour	Prediction of a preterm delivery using a single cervical measurement
Risso et al	Am J Obstet Gynecol	1996	108	Threatened prem labour	Assessment of risk of a preterm delivery with TVS and fetal fibronectin
Hasegawa et al	J Matern Fetal Med	1996	729	15-34 weeks	Prediction of preterm delivery using TVS
Rosenberg et al	Am J Obstet Gynecol	1997	76	Threatened prem labour 24-34 weeks	Prediction of preterm delivery: comparison of TVS and fetal fibronectin
Guzman et al	Am J Obstet Gynecol	1997	10	15-22 weeks	Natural history of cervical change in cervical incompetence
Cetin and Cetin	Eur J Obstet Gynecol Reprod Biol	1997	65	Threatened preterm labour	Prediction of preterm delivery
Sherif and Shalan	J Obstet Gynaecol Res	1997	69		Detection of cervical change during fundal pressure and straining
Guzman et al	Am J Obstet Gynecol	1997	89	15-24 weeks	Detection of cervical change during fundal pressure, coughing and standing
Berghella et al	Ultrasound Obstet Gynecol	1997	43	16-28 weeks	Detection of cervical funneling and the risk of preterm delivery
Rizzo et al	Ultrasound Obstet Gynecol	1998	92	PPROM; 24-32 weeks	Assessment of risk of preterm delivery using TVS and amniocentesis
Rizzo et al	Ultrasound Obstet Gynecol	1998	144	Threatened preterm labour	Assessment of risk of preterm delivery using TVS and amniocentesis
Heath et al	Ultrasound Obstet Gynecol	1998	2702	23 weeks	Comparison of cervical length to past Obstetric history
Heath et al	Ultrasound Obstet Gynecol	1998	2567	23 weeks	Prediction of preterm delivery
Taipale and Hiilesmaa	Obstet Gynecol	1998	3694	18-22 weeks	Prediction of preterm delivery
Arinami et al	J Matern Fetal Med	1999	683	26-28 weeks	Prediction of preterm delivery: comparison with nipple stimulation, granulocyte elastase and fetal fibronectin
Yost et al	Obstet Gynecol	1999	60		Pitfalls of TVS in predicting preterm delivery
Shalev et al	Ultrasound Obstet Gynecol	1999	120	Threatened preterm labour	Assessment of the upper and lower cervix: changes during contractions

The publications of longitudinal data are particularly comparable to my research; the most comprehensive study being done by Iams et al, published in 1996. Almost 3000 women were scanned at 22-24 weeks and then 2531 returned for a further scan four week later. This was not a specifically high risk population, although 16% of those recruited had had a previous preterm delivery. Some shortening of the cervical length between 24 and 28 weeks was shown by Iams et al (35.2 mm to 33.7 mm), corresponding to the reduction in cervical length throughout the third trimester shown in our study (Figure 4.3). The most significant finding from the Iams study was the increasing risk of a preterm delivery with the reduction in cervical length as measured at the 24 week visit. Again, this was mirrored by the Southmead research, with the cervical length at 21-23 weeks correlating with the chance of a preterm delivery (Table 5.3). The next largest series published was presented by Heath et al (1998), but this dealt with a single ultrasound measurement of the cervix at 23 weeks gestation. Again, an association between a short cervix and the risk of a preterm delivery was clearly shown.

Looking at research into elective cerclage and cerclage after ultrasound-indicated cerclage, several papers have been published looking at outcome differences between the two groups (Table 5.16). Guzman et al (1998) compared two groups with poor obstetric histories, 81 of whom had an elective cerclage and 57 of whom were only sutured on the basis of cervical change as seen on TVS. This study very encouragingly showed that, despite the later duration of the suturing (20 compared to 13 weeks) and the cervical change seen on TVS, there was no difference in pregnancy outcome. Berghella et al

(1999) showed no benefit in cerclage, but that was between those who, when cervical change was noted on scan, were either sutured or not at that stage; there was no comparison with an electively sutured group. However, Heath et al (1998) showed a marked difference between the 21 not sutured and the 22 sutured in her series of patients with a cervical length of less than 15 mm; 52% delivery before 32 weeks compared to just 5%. On a slightly different tack, Fox et al (1998) showed an improvement in outcome compared to past history if the decision to suture was based on the cervical appearance on scan. In 19 women with 84% of previous pregnancies ending with midtrimester losses and 62% of third trimester pregnancies delivering before 32 weeks, seven were not sutured as there was no cervical change, and 12 were sutured due to cervical change. In this series only one pregnancy ended before 32 weeks (5%). These relatively small series do suggest that identification of cervical change on TVS is important with regard to the decision as to whether to opt for cervical cerclage, but whether a cervical cerclage after the onset of cervical change is as effective as an elective cerclage at an earlier gestation is still not clear. As stated earlier in this chapter, the differences in gestation at delivery found between the elective and emergency cerclage patients was not significant, but a study of 50 or more patients may have the power to answer the question.

Table 5.16

Publications 1996-1999 regarding cervical cerclage; elective vs. ultrasound indicated cerclage

Author	Journal	Year	Number of patients	Gestation of elective cerclage	Gestation of TVS-indicated cerclage	Comment
Fox et al	Br J Obstet Gynaecol	1998	19	7 not sutured as no cervical change on TVS		No difference in outcome between the two groups
Guzman et al	Ultrasound Obstet Gynecol	1998	138	13 weeks	20 weeks	No difference in outcome between the two groups
Heath et al	Ultrasound Obstet Gynecol	1998	43	21 not sutured	23 weeks	5% delivery before 32 weeks in sutured, compared to 52% in non-sutured
Berghella et al	Am J Obstet Gynecol	1999	63	24 not sutured		All had evidence of cervical change on TVS; no benefit found in cerclage group

Chapter 6

Transvaginal Ultrasound and Cervical Incompetence

Introduction

Recurrent late second or early third trimester pregnancy losses have a variety of causes, one of which is cervical incompetence. The incidence of cervical incompetence is uncertain, with published reports varying from 0.05% to 2% of all deliveries (Grant 1992, Cousins 1980). This wide variation is in part due to the rarity of the condition, but also due to the difficulty and subjectivity in making the diagnosis. A clear, clinical definition was proposed by McDonald in 1980;

'the history (of cervical incompetence is) of one or more mid-trimester abortions, with early rupture of the membranes, usually before the onset of labour. There is absence of significant haemorrhage. The labours are short and relatively pain-free; the fetus is born alive. Repeated middle term miscarriages at the same gestation are significant.'

This definition requires the loss of at least one pregnancy before the diagnosis is contemplated and also requires subjective input, both from the woman herself regarding what is usually a traumatic experience, and also from the Obstetrician involved. There is also evidence that this clinical diagnosis is not completely sufficient; one notable finding from the MRC/RCOG trial of cervical cerclage (1993) was that, in the group in whom there was a clinical diagnosis of cervical incompetence in a previous pregnancy loss, no demonstrable benefit was found by the insertion of a cervical suture. The development of alternative approaches to the diagnosis, aiming for objective and reproducible measures of cervical competence during pregnancy, may be the way forward.

Transvaginal ultrasound scanning (TVS) has been used for many years to observe the cervix. Original research (Zorzolli et al 1994, Murakawa et al 1993) has demonstrated normal values for the cervical length measured transvaginally, whilst large multicentre studies have shown a correlation between cervical length and the risk of a pre-term delivery (Anderson et al 1990, Iams et al 1995, Heath et al 1998). The interest in TVS with regards to cervical incompetence started with individual case reports and reported series of high risk pregnancies (Joffe et al 1992, Guzman et al 1994, Fox et al 1996). These drew attention to the unusual appearances of an open internal cervical os at rest or in response to fundal pressure (Guzman et al 1994) with a normal cervical shape and external dimensions (Figure 6.1, 6.2). However, these studies have been interventional, with the use of cervical cerclage at the initial appearance of any cervical change, so losing the opportunity of observing whether the unusual cervical appearance seen is progressive and therefore potentially diagnostic of cervical incompetence. We performed an observational study of the cervix in those women at high risk of pre-term delivery to determine what further cervical changes, if any, occur in the cervix after the initial appearance of an open internal os.

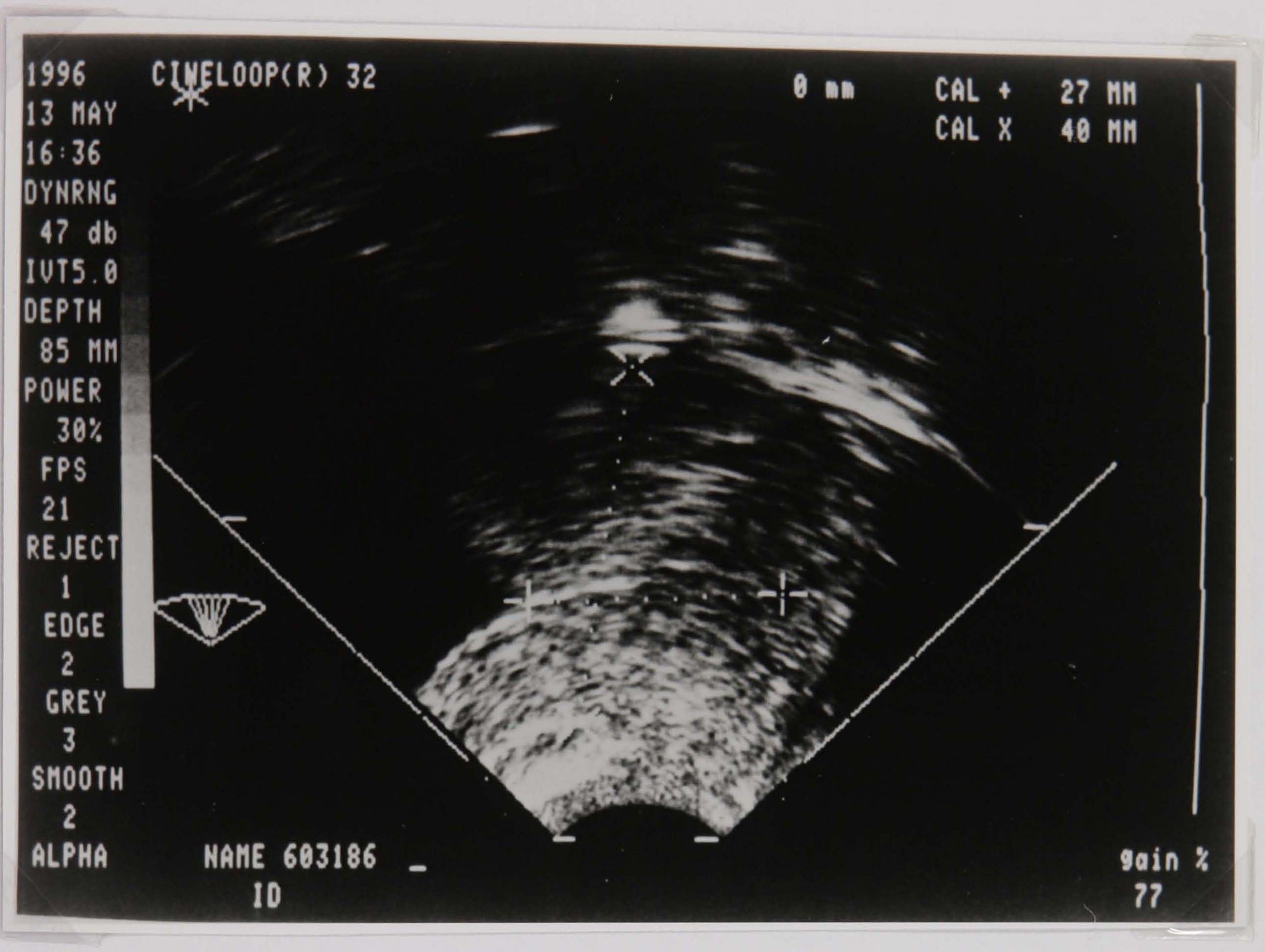


Figure 6.1

A cervix on TVS at 24 weeks gestation. The calipers (+-----+) delineate the cervical length of 27 mm. Although short, the cervical canal is closed.

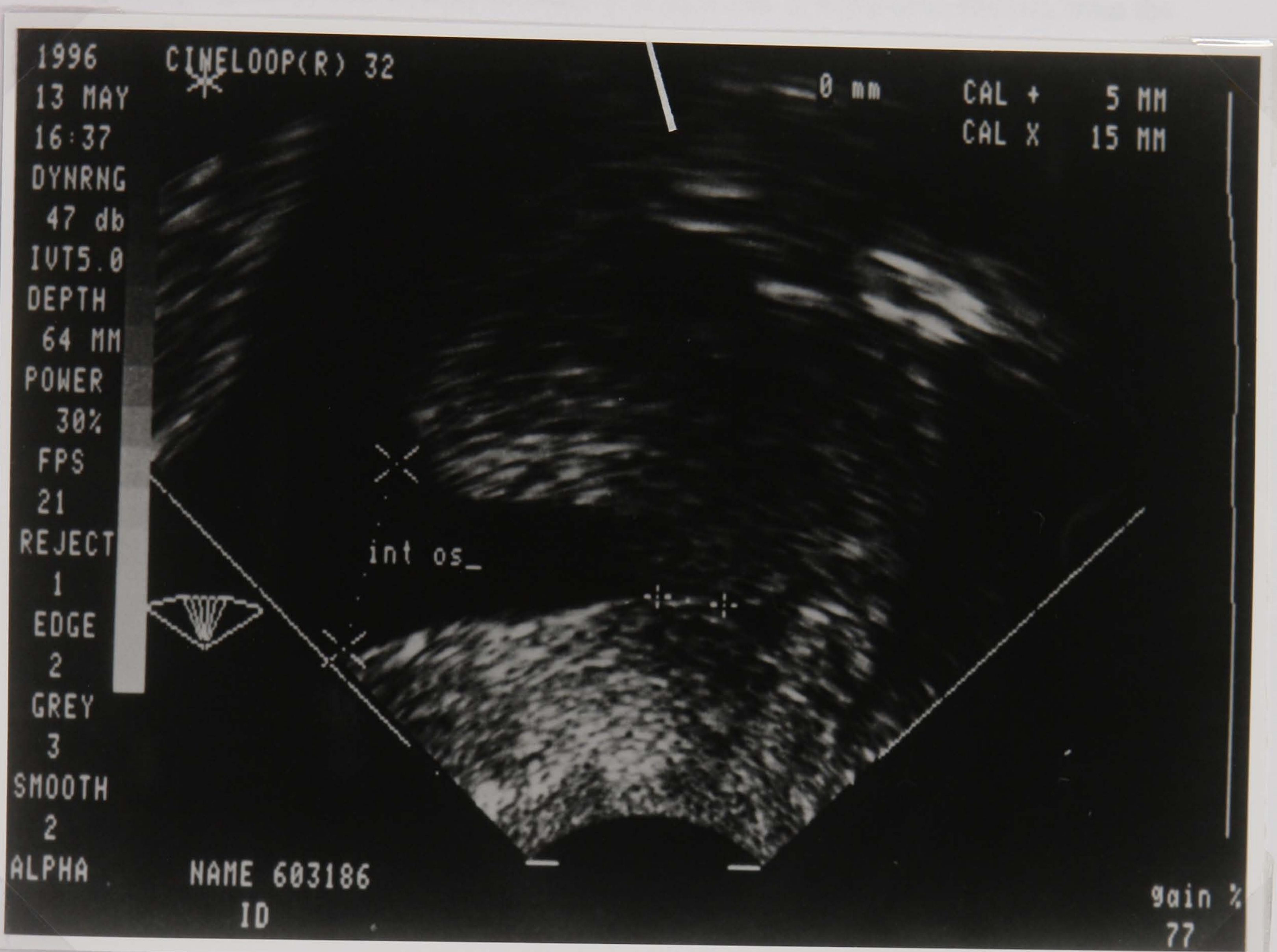


Figure 6.2

The cervix in Fig. 6.1, one minute later, after manual pressure to the fundus of the uterus. The internal os (x-----x) has opened in response to the increased intrauterine pressure, and the closed cervical canal (+------+) now measures just 5 mm. Note there is no change in the external cervical shape, which is what would be felt on digital vaginal examination.

Methods

As part of the larger study investigating the cervical appearance on TVS throughout pregnancy, 106 women considered at high risk of a pre-term delivery from the history taken at the antenatal clinic booking appointment were followed through pregnancy from the second trimester to delivery with serial transvaginal scans of the cervix (Chapter 5). The definition of 'high risk' was adapted from the risk scoring system of Holbrook et al (1989) and described in Chapter 2 (Table 2.1). The recruitment and scans performed are described in Chapter 2.

The aim of the study was to observe any cervical changes without, as far as was possible, any intervention. Agreement was reached with the consultants at Southmead Hospital that all measurements were to be known only to the ultrasonographer (RDM) unless the cervical length, at rest or in response to pressure on the uterus, fell below an arbitrarily set 10 mm (average cervical lengths on TVS in previous studies in second or early third trimester being reported as between 35 and 45 mm (Zorzolli et al 1992, Anderson et al 1990, Iams et al 1996, Kushnir et al 1990, Heath et al 1998)). At this stage the consultant was informed of the measurements and a decision taken regarding future management. Ethical committee approval was obtained for the study.

Results

Of the 106 women in the high risk group, 13 demonstrated an open internal os at rest, or cervical change (cervical shortening or opening of the internal os) in response to fundal pressure at or before 24 weeks gestation (Figure 6.1, 6.2) - 12.2% of the high risk population. (In a cohort of 51 women at low risk of a preterm delivery being studied at the same time, none had had this cervical appearance on ultrasound at or before 24 weeks gestation). Two of the 13 were scanned just prior to an elective cervical cerclage procedure; in one individual the scan showed a normal external cervical appearance but a widely dilated internal os and a cervical length of 7 mm, whilst in the other the cervix appeared normal immediately prior to the cerclage, but two weeks after cerclage had an open internal os with protrusion of the amniotic membranes into the cervical canal. However as the intervention had been planned prior to the scan, both were excluded from the present discussion. The collective past obstetric history of the remaining 11 is shown in Table 6.1.

Table 6.1

Combined past obstetric histories of the 11 women with cervical change on TVS

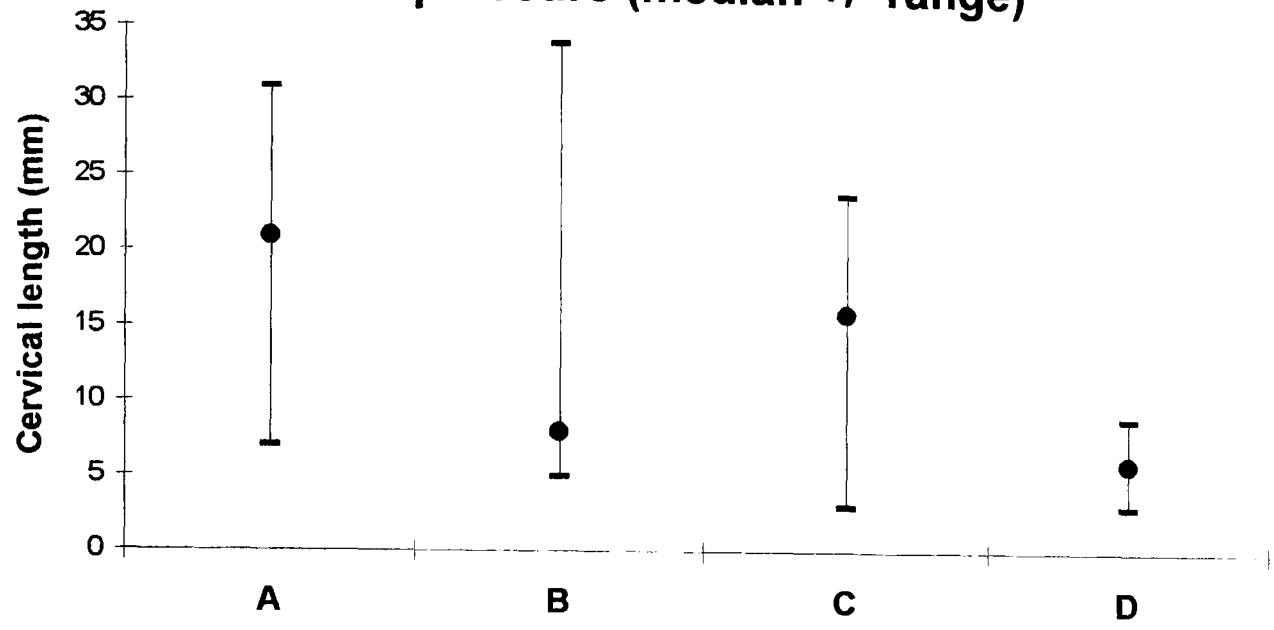
Terminations of pregnancy	9	2 women had 3 terminations each
First trimester losses	2	
Second trimester losses	8	Median: 21 weeks Range: 17-23 weeks
Pre-term deliveries	8	Median: 29 weeks Range: 24-35 weeks
Term deliveries	1	
Median gestation of all deliveries (2nd and 3rd trimesters)	24 weeks	

The median gestation of delivery of any previous pregnancy going beyond the first trimester in this group was 24 weeks, with a total of eight late second trimester losses, six preterm deliveries and just one term delivery (93% preterm deliveries). This compares with the remaining 93 in the 'high risk' group, where the mean gestation of past pregnancies going beyond the 1st trimester was 33.5 weeks, with 61.7% of these 188 pregnancies ending with a preterm delivery. Those with cervical change on TVS in the second trimester were, on past history alone, at markedly higher risk of a preterm delivery in this pregnancy than the remainder of the high risk group.

Cervical change was defined as opening of the internal os at rest or in response to fundal pressure such that there was beaking of the internal os of more than 5 mm and protrusion of amniotic membranes into the cervical canal, or shortening of the measured cervical length of more than 5 mm. The time of onset of this abnormal cervical appearances varied from 14 to 24 weeks (median = 21 weeks). In only three cases was the protrusion of amniotic membranes into the cervical canal present at the first visit; the remaining eight had a normal cervical appearance on TVS on at least one occasion.

At the onset of cervical change the median cervical length in this group was 21 mm (Fig. 6.3 at time point A). Following fundal or suprapubic pressure, the median cervical length fell to 16 mm (C: Fig. 6.3). In two women the application of pressure on the uterus produced no change; one who was first seen at 24 weeks, with a widely dilated internal os and a closed cervical length of 8 mm; the other had marked herniation of amniotic membranes into the cervical canal, an appearance which was present at rest at the onset of each scan.

Figure 6.3 - Cervical change in response to fundal pressure (median +/- range)



A = Cervical length at the initial recognition of cervical change.

B = Cervical length just prior to cervical cerclage.

C = **A** with fundal pressure

D = **B** with fundal pressure

Cervical change was highly significant between the initial scan after fundal pressure (**C**) and the final scan with fundal pressure prior to consideration of cerclage (**D**) (p=0.001; paired t-test, 95% Confidence intervals (CI) 4.1-11.7)), but not between the two comparable scans without fundal pressure, **A** and **B** (p=0.1; CI -1.3-10.0). The difference in cervical length on each occasion after the application of fundal pressure was significant (**A** and **C**, p=0.01, CI 2.6-9.6; **B** and **D**, p=0.03, CI 8.4-19.6).

The implication is that fundal pressure is needed to demonstrate cervical change most clearly and identify those cervices which may potentially be incompetent. One approach is to consider fundal pressure a cervical "stress test".

In nine of the 11 women, a cervical cerclage was performed. This was done, not at the time the initial cervical changes were noted on scan, but only when the cervical length had shortened to less than 10 mm. The time taken for this progression of cervical change was between two and 17 days. In the other two instances the consultant in charge was informed, as agreed in the protocol, but decided against a cervical suture at 24 and 25 weeks gestation. In all cases the cervical change seen was progressive; the median cervical length fell from 21 mm to 8 mm at rest (A to B: Fig. 6.3), with a reduction after fundal or suprapubic pressure to a final median cervical length of 6 mm (from 16 mm at the initial observation - C to D: Fig. 6.3). The standard appearance following cerclage before and after fundal pressure is shown in Figures 6.4 and 6.4. Of note also is the clinical appearance at the time of cervical cerclage; in seven of the nine cases sutured (78%), the amniotic membranes were either visible within the cervical canal of a patulous cervix, or had protruded to the external os.

Infection is considered a significant factor in preterm labour, and thought to play a part in cervical changes prior to labour. In our cohort, six of the eleven (54.5%) had a positive HVS in pregnancy: three for GBS, one for Streptococcus milleri, one for E.Coli and one for Stapylococcus aureus. However, only one had a positive HVS at or before the onset of cervical change on TVS.

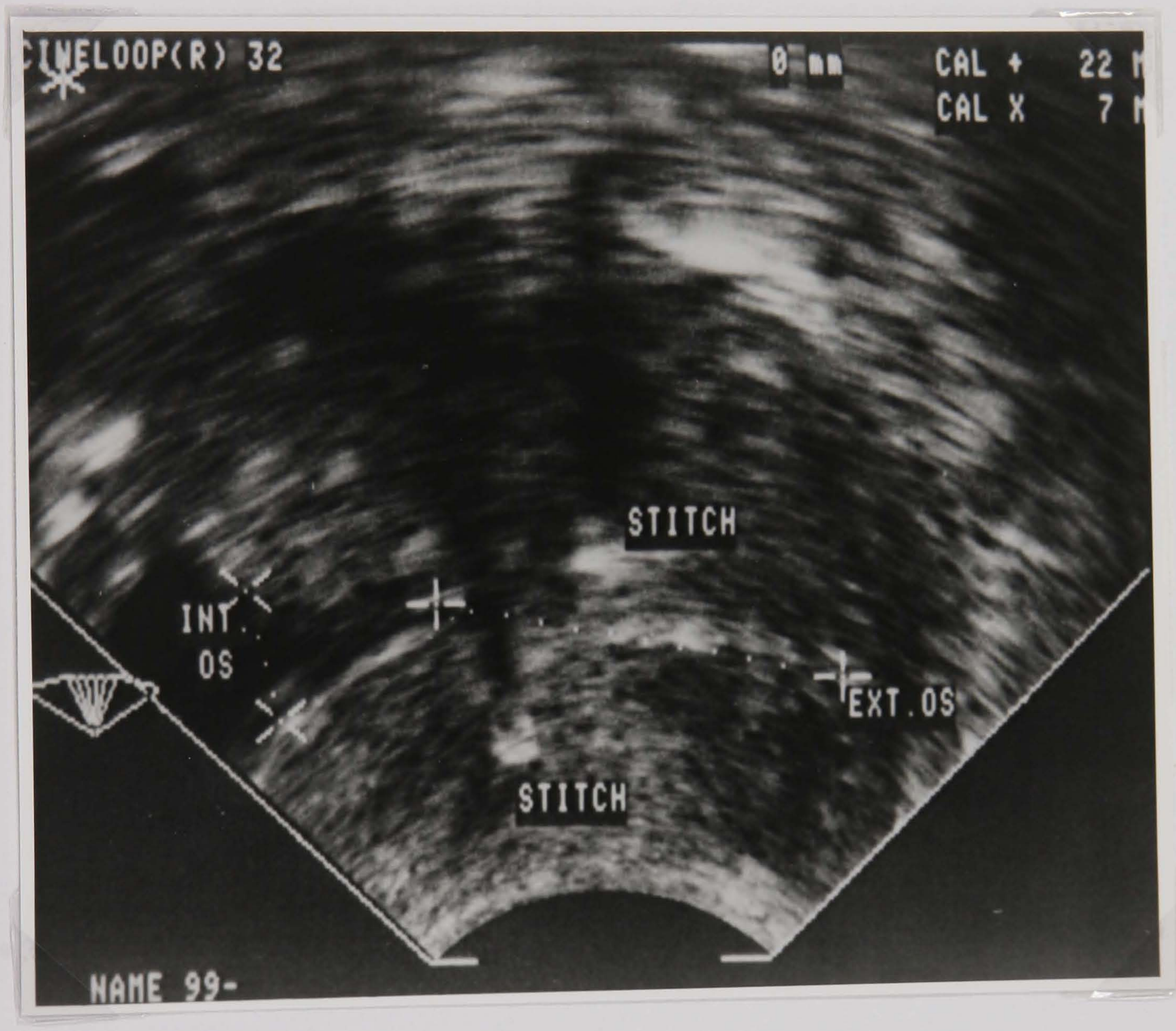


Figure 6.4

A cervix at 26 weeks gestation following cervical cerclage at 22 weeks. The suture can be clearly seen anterior and posterior to the cervical canal.

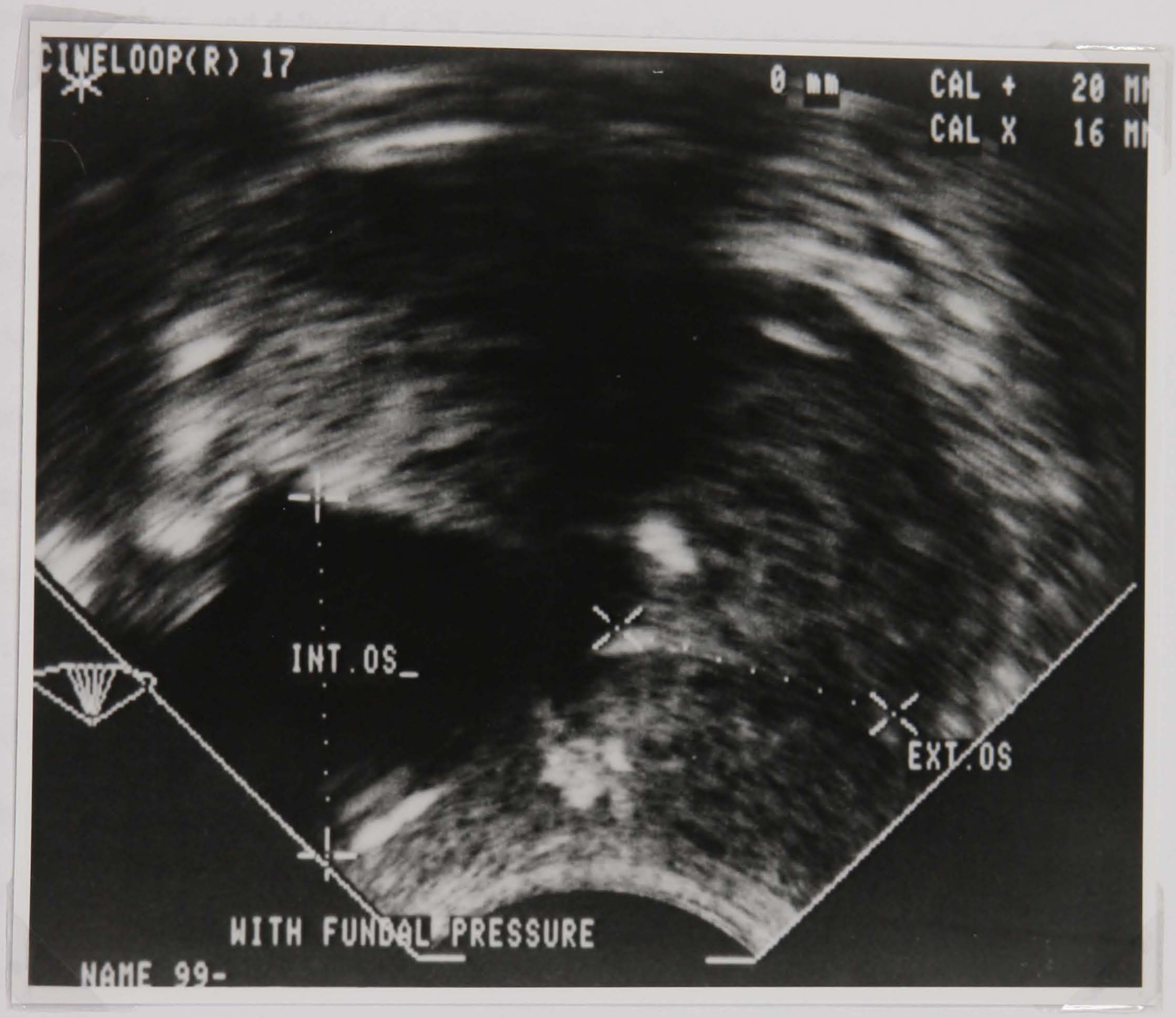


Figure 6.5

The cervix in Fig. 6.4 following fundal pressure. The cervical length (x-----x) has shortened, and the internal os (+----+) opened, but the amniotic membranes have not protruded past the cervical suture.

Ten out of 11 pregnancies ended with a live child. One ended at 18 weeks due to an E.Coli septicaemia following a repeat cervical cerclage, the amniotic membranes having protruded past the original suture inserted two weeks previously. One other had a repeat suture at 23 weeks due to a suture failure, six weeks after the initial cervical cerclage, and delivered at 38 weeks, soon after the suture was removed. In the 10 pregnancies that reached the third trimester, delivery occurred at between 27 to 38 weeks, with a median gestation of 36 weeks, compared to this group's median gestation of previous deliveries of 24 weeks. Of those not part of this study (i.e. the 93 considered high risk for a preterm delivery but without any cervical change on TVS) there were three second trimester losses, 26 preterm deliveries (28% preterm delivery rate), with an average gestation for delivery of 36.4 weeks. In terms of statistical measures, in this group the demonstration of cervical change on TVS had a sensitivity of 0.19 and specificity of 0.94 with regard to a preterm delivery, whilst the positive predictive value (PPV) and negative predictive value (NPV) were 0.64 and 0.68 respectively. If a cut off of delivery under 32 weeks gestation is used (more relevant in terms of neonatal morbidity and outcome), the sensitivity of cervical change predicting a delivery under 32 weeks is 0.25, the specificity 0.92, positive predictive value 0.36 and negative predictive value 0.87.

Discussion

Cervical incompetence has always been a difficult and subjective diagnosis. The treatment usually proposed (cervical cerclage) is invasive, inconvenient for the patient, and carries a significant morbidity and a potential mortality (Grant 1992). There is a need for a method of cervical assessment which identifies which patients might benefit from a suture and equally importantly, in whom it would be ineffective and hence unnecessary. Previous attempts to identify the incompetent cervix, particularly using digital or speculum examinations, have not been successful, and TVS has been shown to be more effective than digital examination in the prediction of a pre-term delivery (Gomez et al 1994). Transvaginal ultrasonography has several advantages in the assessment of the cervix; it is safe in pregnancy, acceptable to the women involved, and the measurements taken are reproducible with little error (Zorzolli et al 1992), and changes in the internal os, not detectable on speculum or digital examination, can be clearly visualised (Guzman et al 1995).

A short cervical length measured on TVS does appear to be a significant risk factor for a pre-term delivery (Iams et al 1995). However we would contend that there is a major difference between a short, though closed, cervix (Fig. 6.1) and one in which the membranes protrude into the cervical canal (Fig. 6.2). The presence of muscle fibres within the uterus and to a lesser extent in the cervix does mean that the appearance of the cervix is not static, but will vary over time. The aim of this study was to see whether one specific cervical appearance, notably the opening of the internal cervical os and protrusion of membranes into the cervical canal, is a transitory phenomenon or a permanent and progressive one which requires treatment. In our cohort of high risk women, the appearance of cervical change prior to 24 weeks was progressive in all cases to a cervical length of less than 10 mm over time (2 to 17 days). Visible membranes within or beyond the cervical canal in the absence of uterine contractions is commonly taken as the clinical appearance of cervical incompetence. This describes what was seen in seven of those nine women in this series who were sutured, and implies that the late TVS appearance (a cervical length less than 10 mm) is equivalent to the usual clinical diagnosis of cervical incompetence. The finding that cervical change seen on TVS prior to 24 weeks appears to progress on to the cervical length of less than 10 mm suggests that an open internal os, at rest or in response to fundal pressure, is likely to be the ultrasonographic appearance of cervical incompetence.

The sensitivity and specificity of the test demonstrates what intuitively one would expect. A low sensitivity of 0.19 (or 0.25 if investigating the more clinically relevant question of deliveries before 32 weeks), even in this high risk group, would tend to imply this may not be a worthwhile screening test on a low risk population, but the identification of cervical change is associated with a high chance of a preterm delivery, as shown by the high specificity of the test (0.94).

One note of caution needs to be identified from our cohort; of the 11 with cervical changes, only nine received a cervical cerclage. Of the two that were observed without cerclage (a decision made by the consultant in charge), one delivered at 30 weeks after a rapid labour, and the second at 37 weeks gestation. This second patient arrived in hospital after reporting a mild backache for the day, was found to be 8 cm dilated on admission and delivered shortly afterwards. This relatively 'silent' labour could be taken to imply that the cervix dilated with minimal uterine contractions; perhaps a partially incompetence cervix with delivery occurring at term? I would contend that all 11 women in this cohort had cervical incompetence, but manifested its effect to varying degrees.

Transvaginal ultrasound offers what I believe to be an objective method of diagnosing cervical incompetence, which at present is a difficult and subjective diagnosis on clinical grounds. Potentially its application will enable more specific targeting of treatment, and also more scientifically based research into therapeutic measures such as cervical cerclage.

Recent Publications

One particular paper since 1995 has looked into the issue of the natural history of cervical change without the initial intervention of cervical cerclage (Guzman et al 1997). By chance Guzman et al also used a cut-off of 10 mm in cervical length before intervention with a cerclage in an effort to observe the cervical changes prior to cerclage. Guzman reported a small study of 10 women found after running a high risk pregnancy clinic for three years, in whom there was cervical change in response to fundal pressure. Progressive cervical changes followed the initial observation, mirroring our results, and all were sutured with the cervical length falling below 10 mm in all cases. On a slightly different tack, Heath et al (1998b) showed there to be a significant risk of a preterm delivery with a short cervix (under 15 mm), and in a non-randomised series of 43 patients (22 sutured, 21 not sutured) there was a marked benefit in cerclage in these patients (5% delivery before 32 weeks compared to 52% in the non-sutured 21 patients). The potential repercussions from this observation is that it may not be the opening of the internal os which is relevant to treatment, but the absolute length of the cervix as measured on TVS.

Should cervical sutures be put in before the cervical length falls to 10 mm? On the basis of Guzman's publication (1997) and this study, provisionally yes; opening of the internal os prior to 24 weeks appears to be progressive towards the clinical definition of an incompetent cervix in all cases studied. The fact that two separate observational studies with a combined total of 21 patients (all of whom were identified from populations felt to be at a high risk of a pre-term delivery) produced very comparable results and equivalent conclusions is, I believe, of significance. Both studies demonstrated progressive shortening of the cervix in these women over time, both showed the importance of fundal pressure in identifying the incompetent cervix, and in both the majority of patients at the time of cervical cerclage had membranes visible within or beyond the cervix.

Ideally, before wholeheartedly recommending intervention in this situation a randomised trial investigating the role of cervical cerclage in women with a short cervix or an open internal os would be complete. Following on from Heath' publications (1998a and 1998b) there is underway a randomised trial into cervical cerclage, basing the intention to treat on the cervical length as measured on TVS at 23 weeks; potentially a clearer picture as to who will benefit from cervical cerclage may appear.

Chapter 7

The Cervical Appearance at Induction of Labour at Term and beyond: A comparison of cervical length on TVS and Bishop score in predicting the induction to delivery interval

Introduction

Induction of labour is a regular occurrence, for a variety of reasons; maternal illness (hypertension, bleeding or diabetes), fetal concerns (particularly growth retardation) or maternal request. The commonest indication, however, is "post term" pregnancy; when delivery has not occurred two weeks or more beyond the expected date of delivery. This has come about with the observation that there is a higher rate of intrapartum stillbirth and early neonatal deaths, commonly related to meconium aspiration or perinatal asphyxia, in those neonates who are still in-utero over 2 weeks (294 days gestation) beyond their expected date of delivery (Crowley 1992b). The reported incidence of pregnancy going beyond 42 weeks gestation varies between 4 and 14% (Crowley 1992b), although the incidence can be reduced (probably because it is more accurately defined) using ultrasound rather than menstrual dates to calculate the estimated date of delivery.

Routine induction of labour involves an initial cardiotocograph to assess fetal well-being, a cervical assessment, usually using the Bishop score (Bishop 1964) and the initiation of labour either using prostaglandin pessaries to promote cervical dilatation and effacement or the rupture of membranes followed by an oxytocic infusion to stimulate contractions. The Bishop score however, was initially developed by Edward Bishop to predict the likely onset of labour and the appropriate time for induction, not as an assessment of the ease or otherwise of the induction process (Bishop 1964). Investigation of the various constituents of the Bishop score (cervical dilatation, cervical length and consistency, cervical position and the station of the fetal head) has consistently shown the cervical dilatation to be of most relevance in predicting the outcome of an induction of labour (Lange et al 1982, Bremme and Nillson 1984, Lyndrup et al 1992, Fuentes 1995, Williams et al 1997). The limitation in the Bishop score's ability to predict outcome is in part due to subjective nature of the examination and also due to variation between individuals, but also may be due to the fact that a digital cervical assessment is based around the external os, whilst the changes during effacement and early labour appear to occur around the internal os with drawing up of the cervix into the lower uterine segment (Fig. 7.1), a change which is easily assessed using transvaginal ultrasound but difficult if not impossible to determine in primiparous women, and can be a potential source of confusion in multiparous women, where the external os is often open but the internal os remains closed.

Several studies have compared the Bishop score to the cervical appearance on transvaginal ultrasound (TVS) prior to induction (Paterson-Brown et al 1991, Boozarjomehri et al 1994, Watson et al 1996, Gonen et al 1997). Boozarjomehri et al found cervical appearance, particularly the presence or absence of a "wedge" or opening of the internal os on TVS was strongly correlated with a reduced induction-to-delivery interval and was a better predictor of ease of induction than the Bishop score. However the women being induced in this study were at term (over 38 weeks, with an average gestation of 40 weeks) rather than post term. Neither Gonen et al nor

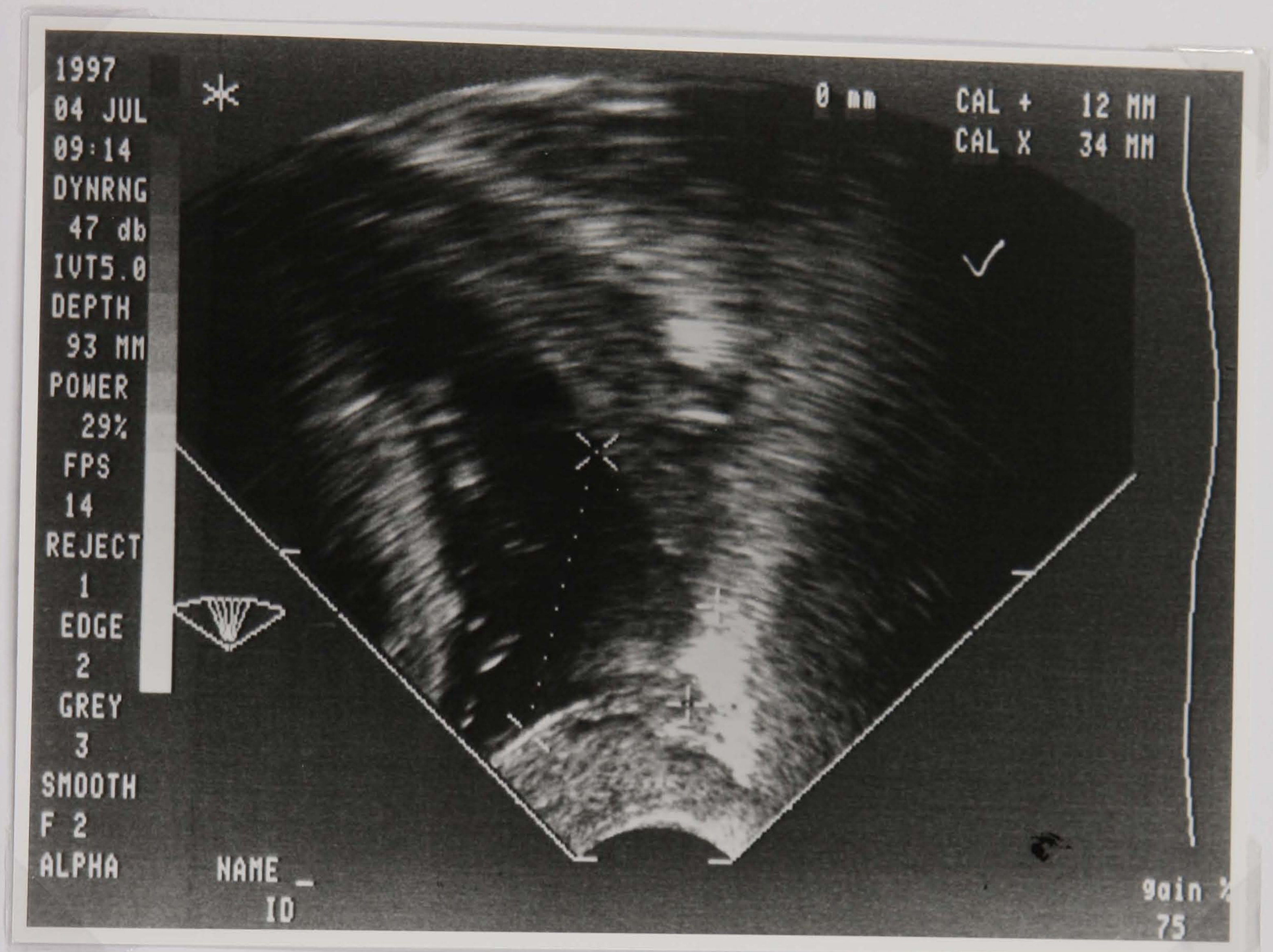


Figure 7.1

A transvaginal scan of the cervix of a woman in her first pregnancy, 12 days beyond her due date. In comparison to the square box-like appearance of the cervix early in the third trimester (Fig. 4.1), beyond the due date there is commonly a loss of the rectangular cervical shape, with wide dilatation of the internal os (x----x). The external os is 1 cm dilated (+----+). This is the transvaginal scan appearance of cervical effacement.

Watson et al found any benefit of transvaginal ultrasonography over a traditional digital vaginal assessment, but neither differentiated between primiparous and multiparous women. Paterson-Brown came to the conclusion that a combination of TVS and the Bishop score was the most accurate method of determining the induction outcome. However the outcome measure was the avoidance of a Caesarean section rather than the ease (or otherwise) of the initiation of labour, and a meta-analysis of studies has suggested that induction of labour does not increase the incidence of Caesarean section or, in post term pregnancies, the likelihood of an operative delivery (Crowley 1992b). Hence using Caesarean section as the outcome measure is perhaps not the most relevant. Comparison of the initial cervical assessment (by vaginal examination or TVS) to the time taken from induction to delivery seems a more relevant method of determining the most appropriate method of cervical assessment prior to induction of labour.

Study Design

At Southmead Hospital the policy is to offer induction of labour to all women who are 12 or more days beyond their expected date of delivery (EDD). The EDD is calculated either from known menstrual dates of a regular cycle when no combined oral contraceptive contraception have been taken for 3 months, or from the estimated fetal age at the earliest ultrasound scan performed if menstrual dates are uncertain or there are more than seven days discrepancy between the menstrual and ultrasound calculated EDD.

All women admitted for induction of labour were given an information sheet regarding induction from the Antenatal Clinic. On the day of induction the women are admitted to an antenatal bed and have the routine observations made (blood pressure, pulse, temperature and cardiotocograph (CTG) reading for 20 minutes). If the CTG is satisfactory and the induction is "routine" (i.e. in line with hospital policy; term +12 days with no antenatal complications) then the midwife looking after the individual woman will perform a vaginal examination and make a decision as to whether a prostaglandin E_2 pessary is appropriate, or whether an artificial rupture of membranes (ARM) would be feasible. For all those women being induced earlier than 12 days after their EDD or with any complications of pregnancy, the medical staff are asked to review, assess and perform the initial vaginal examination. Women in both groups (midwifery or medical staff led inductions) who were beyond their EDD were included in the study.

Setting

All scans were performed in the Cotswold Centre for Women's Health, Southmead Hospital on an Ultramark 4-Plus ultrasound scanner, using a 5.0MHz transvaginal scanner, and a 3.5MHz linear sector transabdominal scanner.

Method

All women being induced after their EDD were seen by the author and the indication for induction of labour and the potential risks and benefits were discussed again. Provided the individual woman was happy to go ahead with the induction, the study was explained and verbal consent for a single transvaginal scan prior to the first vaginal examination was obtained.

The transvaginal scan was performed as described in Chapter 2. In the majority of cases the subsequent vaginal examination and assessment of the Bishop score was performed by a member of staff other than the author in order to make it objective with regards to the vaginal ultrasound scan, although on a few occasions the Bishop score was, because of hospital policy, performed by the author not the midwifery staff.

Study Duration

February 1997 - August 1997

Results

A total of 51 women agreed, after discussion, to be involved in the study. One was scanned and then decided against proceeding with the induction of labour so was discounted from the results. 26 women were in their first ongoing pregnancy, whilst 24 were in a second or subsequent ongoing pregnancy. Of the multiparous women, the mean number of days beyond the EDD at presentation was 10.8, with a median of 12 (range 4 - 15 days). In the nulliparous women, the mean distance beyond the EDD at presentation was 12.2, with a median of 12 (range 8 - 17 days).

Induction and Delivery results

The primiparous women required on average 1.6 prostaglandin pessaries for the induction of labour, whilst the multiparous women used an average of 1.3 pessaries (unpaired t test, t = 0.93: not significant). The induction-to-delivery interval in the primiparous women was an average of 23.8 hours, significantly longer than the 16.1 hours in the multiparous women (Table 7.1). The modes of delivery are summarised in

Table 7.2, there being significantly more operative deliveries in the primiparous women. The mean birthweight in the group was 3659g (range 2400-4850).

Table 7.1

Comparison of primiparous and multiparous women

	Prostin pessaries				Induction-to-delivery interval (hours)			
	Mean	Median	sd	Range	Mean	Median	sd	Range
Primps	1.6	2	0.8	0 - 3	23.8	13.2	13.9	8 - 55.8
Multips	1.3	1	1.0	0 - 5	16.1	13.2	11.4	3 - 54.7
Unpaired t test	t = 0.93 p = 0.36				t = 2.13 **p = 0.038**			

Table 7.2

Modes of Delivery

Type of Delivery	**Total Number**	**Multiparous women**	**Primiparous women**
Normal vaginal delivery	38 (76%)	23 (96%)	15 (58%)
Emergency Caesarean section	5 (10%)	1 (4%)	4 (15%)
Ventouse	4 (8%)	0	4 (15%)
Forceps	3 (6%)	0	3 (12%)

There was no difference in the mean cervical length, width or opening of the internal os between multiparous and primiparous women (Table 7.3), confirming the findings earlier in pregnancy (Chapter 4). Nor did the pre-induction respective Bishop scores differ significantly (primips; mean = 5.3, sd = 1.9: multips; mean = 5.1, sd = 2.1).

Table 7.3

Cervical Measurements: Primips vs Multips

	Mean cervical length (sd)	Mean cervical width (sd)	Mean cervical beaking (sd)
Primips	16.3 mm (12)	55.6 mm (10)	2.6 mm (2.3)
Multips	16.8 mm (9.4)	55.6 mm (8.7)	2.3 mm (2.1)

Multiple Linear Regression

As there was a significant difference in the induction to delivery interval between primiparous and multiparous women, it would seem advisable to deal with the two groups separately for comparison of the cervical assessment methods to the induction to delivery interval.

The induction to delivery interval for both primiparous and multiparous women was Normally distributed, so linear regression analysis was appropriate. The variables compared against the induction to delivery interval are shown in Table 7.4. Stepwise multiple linear regression in the primiparous women against the induction to delivery interval showed cervical length to be the only independent variable with regard to the induction to delivery interval. In the multiparous women, multiple linear regression demonstrated no significant association between any cervical measures (ultrasound or Bishop score) and the induction to delivery interval.

Table 7.4

Multiple Linear Regression Analysis against induction-to-delivery interval: Primiparous Women

Variables used in linear regression analysis
Number of days beyond EDD Cervical length Cervical width Cervical beak 1st Bishop score Birthweight

	Induction to Delivery Interval (hours)		
R^2 value	**0.33**		
	B Unstandardised Coefficients	**95% Confidence Intervals**	**p value**
Constant	12.90	5.26 to 20.54	
Cervical length	0.67	0.28 to 1.06	p = **0.02**

Discussion

Induction of labour is common in modern Obstetric practice, with up to 25% of all labours being induced (St. Michaels Hospital audit, 1998). A prediction of the likely length of time between the induction and delivery is useful both for the patient and also the obstetrician. It could help prepare the patient for the probable time to delivery, and also help in planning when to start induction in order to minimise out-of-hours work and the risks that such work can entail, as highlighted in several CEPOD reports.

Bishop scoring of the cervix is subjective and has limitations, but is at present the basis of cervical assessment prior to induction. From the information presented in this study, it would appear that in primiparous women only, cervical assessment using transvaginal ultrasound to measure the cervical length is more effective at predicting the induction to delivery interval than the standard Bishop score. More recent publications (Watson et al 1996, Gonen et al 1998) have also investigated this area and will be considered at the end of this chapter.

The data from this study is at variance with the results from Boozarjomehri et al (1994), who found an association between the opening of the internal os and the induction to delivery interval; in our results no such association was found. However, as has already been shown (Chapters 4 and 5) there is wide variation between and within individuals with regard to the opening of the internal os, making accurate assessment based on that particular measurement difficult.

In multiparous women, the lack of correlation of any form of measurement to the induction to delivery interval is, intuitively, not surprising. The multiparous cervix appears to respond to labour and contractions very differently (and with greater variability) than the primiparous cervix, with rapid cervical change in terms of length, effacement and dilatation in response to contractions being commonplace. Hence it is unsurprising that no cervical measure was found to adequately predict the time until delivery.

Looking from a practical viewpoint, how can the use of TVS in cervical assessment improve practice? One of the main concerns identified by the CEPOD reports has been the increased incidence of poor outcomes associated with out-of-hours surgery, and this can also be applied to Obstetrics with regard to operative vaginal deliveries and Caesarean sections. Also, the reduced availability of Paediatric and laboratory staff, and the reduced midwifery and Obstetric staff available out-of-hours makes planning for deliveries within daylight hours advisable. There is insufficient data presented here to be able to satisfactorily answer that question, but the results of the multiple linear regression analysis would suggest a larger randomised study basing the timing of induction on either the Bishop score or the cervical length on TVS would be of benefit.

Recent Publications

Following the onset of our research at Southmead, just two studies have been published looking at a comparison of cervical length on TVS and Bishop score with regard to the prediction of outcome of induction of labour (Table 7.5).

Table 7.5

Publications 1995-1999
Comparison of cervical length to Bishop score in predicting outcome of induction of labour

Author	Journal	Year	Number of patients	Comment
Watson et al	Obstet Gynecol	1996	109	Cervical dilatation the only predictor
Gonen et al	Eur J Ultrasound	1998	86	Bishop score better predictor than cervical length

Neither Watson nor Gonen found any benefit of TVS over the standard Bishop score. In particular, Watson et al found that, of the components of the Bishop score, only cervical dilatation was predictive with regard to the outcome of the induction of labour. This conclusion has been mirrored by several studies looking specifically at the Bishop score alone and its components (Lange et al 1982, Lundrup et al 1992, Fuentes et al 1995, Williams et al 1997). However, both Gonen and Watson made no distinction between primiparous and multiparous women, a distinction which is necessary as shown by the data in this research. As the cervical length on TVS is only of relevance in primiparous women in the Southmead research, neither of the larger more recent publications can be said to refute our conclusions.

Chapter 8

Conclusion

Introduction

As with all new modalities for investigating the human body, intra cavity ultrasound and particular transvaginal ultrasound has been used in many different fields. With all the different uses, it is important to endeavour to distinguish those uses which are of benefit and those which have a limited value. The intention of this thesis was to look at the use of TVS throughout pregnancy in several different scenarios, aiming to find out those which might have clinical relevance.

Early Pregnancy

The aim of scanning in early pregnancy was to see whether the cervical appearance in the first trimester could predict the pregnancy outcome in a way that second and third trimester scanning has been demonstrated to be of use (Iams et al 1996, Heath et al 1998). From the numbers collected in this trial, no association could be found between the cervical appearance in the first trimester and the pregnancy outcome. The power calculation in Chapter 3 suggests that a relatively small study, correctly done, could have the power to demonstrate a significant difference in cervical length between term deliveries and preterm deliveries, even at this gestation. A repeat of this study with larger numbers would seem appropriate. It may however not be so fruitful to investigate cervical beaking in the first trimester. It became apparent as more first trimester scans were performed that in most cases, the pregnancy was implanted in the fundus and hence at this stage of pregnancy the lower uterine segment was not distended, but rather was confluent with the cervix (Fig. 3.1). As part of the importance of second or third trimester scanning is the visualisation of any change or beaking of the internal os, a closed lower segment may preclude this sign from appearing.

Second and Third Trimester - High and Low Risk Cohorts

Past research has shown several potential benefits of scanning in the second and third trimesters, the main advantages being the assessment of risk of a preterm delivery (Iams et al 1996, Heath et al 1998) and the identification of a weak or incompetent cervix (Guzman et al 1994, 1997). Several other associations have been demonstrated from this research.

1. As well as providing a low risk population to compare with the cohort at high risk of a preterm delivery, the data from the low risk cohort showed that the cervical measurements from primiparous and multiparous women were not significantly different, so allowing comparisons to be made irrespective of parity.

2. A past history of miscarriage carried an association with a shorter cervical length at 21-23 weeks gestation in the high risk group, whilst a past history of termination in the high risk population at 18-20 weeks was associated with a significantly shorter cervical length, an association lost in the low risk group once the Bonferroni correction was included. This does bring to mind the consideration of the method of termination, and the possibility that a forcible dilatation of an unripe cervix can cause significant damage. Potentially hence, the use of prostaglandins for cervical priming prior to surgical terminations and an increased use of medical terminations does become increasingly important. Investigation of this with regard to the future risk of a preterm delivery would seem worthwhile.

3. The multiple linear regression analysis in both the high and low risk cohorts did demonstrate that cervical length and, importantly, change in cervical length over time, was positively associated with the gestation at delivery, with a short cervix and a large shortening of the cervical length between 18 and 26 weeks both correlating with a preterm delivery. The poor sensitivity of both measures in predicting a preterm delivery suggests that, on the basis of the present data, neither can be recommended as a screening test for a low risk population. However, the importance of cervical change over time is a new finding, and warrants further investigation alongside the large trials looking a single cervical measurements at particular gestation (Heath et al 1998). A use of the technique, measuring cervical length, cervical change with pressure of the uterine fundus, and cervical change over time in different populations will hopefully clarify the place the technique might have in monitoring high risk pregnancies and predicting the outcome.

Cervical Incompetence

Cervical incompetence is a diagnosis based largely on clinical history and subjective measures. Transvaginal scanning can clearly demonstrate the cervix from internal to external os, giving an excellent opportunity to observe, if any, the cervical changes that occur with cervical incompetence.

Following through the small group of women who developed cervical changes over time demonstrated several points.

1. The cervical changes seen were rare - even in a population known to be at significant risk of a preterm delivery, only 10% (11 out of 106) had changes in the cervical appearance before 26 weeks.

2. All the cervical changes seen before 26 weeks were progressive, with no case reverting to normal.

3. In those women in whom a cervical cerclage was inserted after the cervical length fell to below 10 mm, the majority (seven out of nine) had membranes visible within or through the cervical canal, a situation in the absence of uterine contractions usually felt to be synonymous with cervical incompetence.

The conclusion to be drawn from this small sample of high risk pregnancies is that the cervical changes seen (Fig. 6.1 and 6.2, 6.4 and 6.5) appear to be the ultrasound appearance of cervical incompetence. Using this as the basis of a diagnosis of cervical incompetence and hence a trial into the use of cervical cerclage for cervical incompetence would seem to be the next step forward.

Cervical Appearance at Induction of Labour

The present cervical assessment prior to induction of labour using the Bishop score is subjective, and the aim of investigating TVS in this scenario was to see whether a more objective and accurate predictor of outcome could be found.

In multiparous women there was no improvement in the prediction of the induction-to-delivery interval in using TVS to measure cervical length compared to using the Bishop score. However, in primiparous women, the only factor that correlated with the induction-to-delivery interval in multiple linear regression analysis was cervical length at induction. The next trial that is needed is a randomised controlled trial basing the timing of the induction on the cervical length on TVS or the Bishop score, the aim being to see which will more accurately reduce the incidence of out-of-hours deliveries and the increased risks associated with such labours.

Future Research Implications

The numbers involved in the first trimester scans were, in retrospect, too small to provide any firm conclusions. As nuchal translucency scanning becomes more universal as a method of screening for fetal abnormality, an audited programme of routine TVS to observe the cervix at the 12 week scan and correlating the findings to outcome might provide the numbers required to demonstrate a relevance of cervical length in the first trimester to the risk of prematurity.

The connection between a short cervix in the second and particularly the third trimester and the risk of a preterm delivery is now well established (Heath et al 1998a, Iams 1997), but the reasons behind this association are not so clear. The research presented here demonstrated a link between a past history of termination of pregnancy and a past history of miscarriage, and both of these could be investigated further, particularly with a prospective study looking at cervical length prior to termination of pregnancy and again in any future ongoing pregnancies. Other known risk factors for a preterm delivery, in particular vaginal colonisation with Group B Streptoccoci, Bacterial Vaginosis or mycoplasma (all of which have been implicated in preterm deliveries) should be looked for in correlation to the cervical length on TVS.

A trial into cervical cerclage with randomisation based on the cervical length on TVS is at present underway, coordinated from Kings' College Hospital. This hopefully is going to be the definitive trial examining the efficacy of cervical cerclage and also the effectiveness of TVS in predicting those who will benefit from intervention. Further research into cervical cerclage and TVS is likely to depend on the results found, but another important area is the timing of cerclage. There is at present conflicting results regarding the effectiveness of cerclage in the early and late second trimester (Guzman et al 1998, Heath et al 1998b, Berghella et al 1999), so further studies into whether late cerclage (after 20 weeks), particularly after cervical change on TVS, is as effective as elective cerclage at 13-14 weeks, will be needed.

With regard to the induction of labour in primips, two alternatives for future research will be to either run a randomised trial, basing the time of induction of labour one or other of the methods of assessment, or to alter Labour ward practice to base induction on TVS findings and compare retrospectively with past data as to times of delivery. Ideally a randomised trial would provide the more comprehensive answer, but in terms of the practicalities of running a labour ward, a retrospective analysis comparing one method to the other may be more workable.

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